DRUG INDUCED PROTEIN BIOSYNTHESIS AND ITS INFLUENCE UPON SULFHYDRIL GROUP AMOUNT IN SOME ORGANS WITH CASES OF ACUTE MERCURY INTOXICATION

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A series of our previous investigations demonstrated the favourable effect of phenobarbital induced protein biosynthesis on some manifestations of the acute and chronic mercuric chloride intoxication. We reported an increase of mercuric chloride LD_{50} value and a considerable reduction of serum urea and creatinine concentrations sharply increased in an acute intoxication (1); a protective effect on the changes of nucleolus formation and the processes of cell division of bone marrow cells determined by mercuric chloride (2); an increased mercury urine excretion with mercury — carriers (3), etc. It is possible that the increased tissue content of proteins containing sulfhydril and other functional groups facilitates the binding and inactivation of mercury ions. The eventual presence of metalthionein, a specific protein responsible for the inactivation of a number of heavy metal ions could be of special importance (6). The inductive nature of this rich in sulfur-containing amino acids protein is a factor which can explain the favourable effects of phenobarbital well known as a powerful inductor of protein and enzyme biosynthesis.

In the present paper we study the influence of preliminary phenobarbital induction of protein biosynthesis upon sulfhydril group contents in kidneys, liver, aortic wall and serum proteins in an acute mercury intoxication conditions. We paid attention to these functional groups because of the basic role they play in rendering harmless the mercury after poisoning with it.

Material and methods

The experiments covered three groups of white male rats: I^{st} — controls treated with saline; II^{nd} — injected with mercuric chloride in a dose of 7,5 mg/kg. s. c., III^{rd} — treated with phenobarbital in a dose of 60 mg/kg intraperitoneally for 3 successive days before mercuric chloride application. Last phenobarbital injection was done 2 h before mercuric chloride applied in the same dose as with the rats of the II^{nd} group.

Sulfhydril group determination was performed 24 h after mercuric chloride injection in serum, liver, kidneys and aorta. The grounds for selection of these organs were reported elsewhere (4). Tissues were homogenized by using bidistillated water to prepare 6,75 per cent liver and kidney homogenates and 1,25 per cent aorta ones. Sulfhydril groups were determined in supernatant fraction obtained by centrifugation with 4000 revolutions per minute for 10 min in serum. Sufhydril group determination was done by using polarographic device LP-60

reconstructed by an additional apparatus for amperometric titration after Ivanov's method (5). Sulfhydril group quantity is presented in mol/mg protein. Protein content of samples was estimated after Lowry's method.

Results and discussion

The results obtained are shown on table 1. It can be seen that mercuric chloride causes a statistically significant sulfhydril group decrease in aorta, kidneys and serum. However, it is statistically unreliable when liver is concerned. This weak effect can be due to the relatively scanty symptomatics originating from this organ in mercury poisoning.

Table 1

Sulfhydril group content in rat liver, kidneys, aorta and serum after separate mercuric chloride injection and phenobarbital induced protein synthesis

Treatment with:	Liver	Kidneys	Aorta	Serum
Saline	$14,6\times10^{-7}$ mol/mg 100,00 %	$11,7\times10^{-7}$ mol/mg 100,00 %	$5,0\times10^{-7}$ mol/mg 100,00 %	$11,3\times10^{-7}$ mol/mg 100,00 %
Mercuric chloride	$12,6\times10^{-7}$ mol/mg 85,86 % $p^{+}>0,05$	$7,0\times10^{-7}$ mol/mg 59,72 % $p<0,001$	$2,3\times10^{-7}$ mol/mg 43,25 % $p<0,002$	$5,6\times10^{-7}$ mol/mg 49,91 % $p<0,025$
Phenobarbital and mercuric chloride	$11,4\times10^{-7}$ mol/mg 77,94 % $p+>0,05$ $p^{++}>0,05$	$8,9\times10^{-7}$ mol/mg 76,11 % $p>0,05$ $p>0,05$	$6,0\times10^{-7}$ mol/mg 119,84 % $p>0,05$ $p<0,025$	$6,5\times10^{-7}$ mol/mg 57,54 % $p>0,05$ $p>0,05$

Note: p+ — comparison with controls injected with saline
p++ — comparison with the animals injected with mercuric chloride

Preliminary phenobarbital induced protein biosynthesis is an antagonist to a different extent to sulfhydril group reduction in aorta, kidneys and serum in mercury intoxication. There is the strongest effect when aorta is concerned. Preliminary phenobarbital treatment causes sulfhydril group content increase even over control level (table 1) in aorta. This effect is especially significant when one takes into consideration that mercuric chloride treatment causes sulfhydril group content reduction to the greatest extent just in aorta. The restitution action of protein induction on sulfhydril group content in kidneys and serum is less expressed, although there is no statistically reliable difference between sulfhydril group contents in control and both phenobarbital and mercury treated animals when these tissues are concerned, too.

In comparison with thiol antidotes (unithiol, dimercaptopropanol and penicillamine) which were previously studied (4) phenobarbital induced protein synthesis has the strongest restoration effect on aortic sulfhydril group contents. Concerning the kidneys, phenobarbital treatment has a weaker effect than thiol antidotes in spite of the lack of statistically significant differences in sulfhydril group contents between the control animals and those treated with mercury and

each substance studied. The favourable effect of protein induction on serum sulfhydril group content is comparable with that of dimercaptopropanol and penicillamine but considerably weaker than that of unithiol (4).

These comparative data show a similarity in the action of approved thiol antidotes unithiol, dimercaptopropanol and penicillamine, on the one hand, and phenobarbital induced protein biosynthesis, on the other, on the reduced organ and serum sulfhydril group content in mercury intoxication. This similarity is namely an other reason to suggest (3) the use of phenobarbital induced protein biosynthesis in the prophylaxis and treatment of mercury intoxication.

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ЛЕКАРСТВЕННАЯ ИНДУКЦИЯ БИОСИНТЕЗА БЕЛКА И ЕГО ВЛИЯНИЕ НА СОДЕРЖАНИЕ СУЛЬФГИДРИЛЬНЫХ ГРУПП В НЕКОТОРЫХ ОРГАНАХ ПРИ ОСТРОМ ОТРАВЛЕНИИ РТУТЬЮ

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РЕЗЮМЕ

Целью исследования является установление влияния предварительной индукции биосинтеза белка фенобарбиталом на содержание сульфгидрильных групп печени, почек, стенки аорты и сывороточных белков в условиях острой интоксикации ртутью. Установлено, что хлористая ртуть вызывает статистически достоверное понижение содержания сульфгидрильных групп в аорте, почках и сыворотке крови. Предварительно индуцированный фенобарбиталом биосинтез белка в различной степени увеличивает сульфгидрильные группы в указанных органах после интоксикации ртутью.