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Extrapolation the effects of pyridoxine and isoniazid solutions from animals to human

Abstract

On the basis of toxicological, physico-chemical and microbiological experimental studies to determine the antidote properties of vitamin B6 in conditions of overdose of isoniazid, the role of vitamin B6 in increasing the specific therapeutic activity of this tuberculostatic, to extrapolate the obtained data to a higher biological object.

Extrapolation of toxicological indices (LD_{50}, Limac) from four species of animals per person showed that they are 8960 for 5% of the solution of pyri-doxin hydrochloride; 127; 1254 mg/kg, respectively, and for 10% solution of isoniazid-1249, 19, 175 mg/kg, respectively. In experiments on guinea pigs for the first time found that the effectiveness of the treatment of destructive tuberculosis drugs with isoniazid and vitamin B_6 is due largely to the optimal dose of vitamin B_6 and depends on the ratio of doses of both drugs

Keywords: tuberculosis, experimental model, isoniazid, vitamin b_6, extrapolation, white mice, white rats, guinea pigs, cats

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Introduction

Previously, new data were obtained on the study of the properties of a 5% solution of pyridoxine hydrochloride in relation to the development of processes of complicated action of 10% solution of isoniazid for intravenous administration in a modular animal experiment. They allowed to reveal the presence of a pronounced protective action, which was attributed to the value of the indicator in the therapeutic and protective index. These toxicological studies indicate the possibility of developing a system of measures for the treatment and antidote effects of pyridoxine on the overdose of isoniazid, which is extremely important in the widespread use of drugs for the treatment of tuberculosis.

Justification ratio of toxic dose of isoniazid (overdose or negligent use) and medical antidote pyridoxine dose (LD_{50} since 0.1 or less), in future, be conducted in different groups of animals to perform extrapolation of results. Obtained in the experiment, from animals to the highest biological object-human.[1,2] Purpose - to prove the possibility of transferring the experimental data to improve performance and reduce the toxicity of isoniazid and its pathogenic antidotes of the animals to a higher biological object-human.

Materials and methods

As an object of the medical-biological study of the influence of physiologically active substances used sexually mature animals, which were kept under standard vivarium conditions. The duration of the study on acute toxic effects in animals complied with GLP guidelines. The withdrawal of animals from the experiment carried out by bleeding through the thigh artery. The works were carried out in special boxes. They were equipped with devices for monitoring and the effects of drug use on experimental animals. All results obtained during experimental studies were grouped, summarized in a table and statistically processed. In the case of statistical processing of materials, the difference between the average was calculated according to the t-criterion of the Student for coordinated and non-consistent levels. When calculating the probable differences in physiological parameters, methods of nonparametric statistics were used.

Extrapolation of action indicators (pharmacological and toxicological) in determining the possibility of extrapolation of data on the therapeutic efficacy of 5% pyridoxine hydrochloride solution to counter overdose of 10% solution of isoniazid was performed according to the standard operating procedure (SOP), which is the last link in the study of the harmlessness of potential toxicants. The SOP regulates the use of funds, as well as the amount of preventive measures for both staff and volunteers or patients during the testing of drugs, as well as defines all the values of active doses and concentration for a person when transported from the experimental material obtained in animals. For better and more efficient extrapolation results, the number of species studied should be maximized. We have determined the importance of toxicometric indices in 4 animal species: white mice, white rats, guinea pigs, and cats.

Discussion

In Table 1 of the 5% pyridoxine solution for controlling the overdose of 10% solution of isoniazid from animals to a higher biological species-human (Table 2) it can be concluded that according to the magnitude of the specific sensitivity coefficient and the relationship between the action of the drug, there is a definite harmonization. It has a certain feature. Its meaning can be reduced to the fact that the effect of remedies on white mice and rats does not have a clear «body weight - the effect of action» agreement. However, the influence on other biological objects (guinea pigs and cats), this dependence is clear. The same dependence exists between small animals (mice, rats) in relation to the larger animal body mass. Based on this circumstance, the transfer of the investigated values of the extrapolation indicators, although it is somewhat approximate, is not only appropriate, but it is possible to obtain an assertion on the biological tolerability of the transfer of medical and biological data from one species to another. The obtained values of mid-life doses of biologically active substances for different species of animals indicate that the predicted value for an average person with a body weight of 70 kg is a figure whose achievement in the real conditions of the experiment is extremely difficult, and in situations involving overdose in clinical practice, practically possible. However, account should be taken of this possibility in the development of a set of measures for the preventive antidote effect of 5% pyridoxine solution to counter overdose of 10% solution of isoniazid.

Table 1 Toxicological indicators of the effect of 5% pyridoxine solution and 10% solution of isoniazid

Indicators	White mice		White rats		Guinea pigs		Cats	
	Pyridoxine	Isoniazid	Pyridoxine	Isoniazid	Pyridoxine	Isoniazid	Pyridoxine	Isoniazid
LD50 mg /kg	1800,0	210,0	1460,0	195,5	2660,0	450,5	5500	650
LD0 mg/kg	257,2	30,1	204,4	27,5	374,6	63,4	797,1	92,9
Limac mg/kg	27,0	3,1	21,9	2,92	34,4	6,8	82,5	9,8
Limxp mg/kg	90,0	10,5	7,3	1,0	11,5	2,3	27,5	3,3

Table 2 Extrapolation of the effects of the 5% solution of pyridoxine and 10% solution of isoniazid from animals to the higher biological object–human

Indicators	LD50	Limac
5% solution of pyridoxine	15200	255
10% solution of isoniazid	1350	37,8

Conclusion

Thus, the results obtained showed some approximate values toxicometry indicators and pointed to the possibility of their use in the development of dose-dependent approaches to sharing 5% solution of pyridoxine and 10% solution of isoniazid.

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None.

Conflicts of interest

Authors declare no conflicts of interest.

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