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Effects of a Snake Venom and Some Hypometabolic Agents on the Substandard Gas-Oxygen Metabolism in Mice

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Abstract: A lethal dose of the snake Vipera lebetina venom decreases the standard gas-oxygen metabolism of mice approximately threefold while its nonlethal dose does so twofold. The same effects on the gas-oxygen metabolism of mice were noted for lethal and nonlethal doses of aminooxyacetate (blocker of aminotransferases), catacin (antihypoxant), halothane (anesthetic agent) and serotonin (hypometabolic agent).

It is concluded that the organism's physiologically reversible substandard metabolic (or vital hypometabolic) limit induced by different intoxications is approximately two times as low, and the irreversible substandard metabolic (or lethal hypometabolic) limit is three times as low as the level of the standard metabolism.

Key Words: Gas-oxygen metabolism, snake venom, intoxication, *Mus.*

Yılan Zehiri ve Bazı Hipometabolik Ajanların Farelerdeki Standard-altı Oksijen-Gaz Metabolizmasına etkileri

Özet: Vipera lebetina yilaninin oldürecek dozdagi zehri farenin gaz-oksijen değişimini estalame üç kere azaltıyor. Öldürmeyecek dozda-gi miktarı ise iki kereye azaltıyor. Gaz-oksijen değişimindeki aynı görünüşteki efekti aminooksiasetat (aminotransferas blokator), katasina (antihipoksant), galotana (anestezi) ve serotonin (hipemetabolit) öldürecek ve öldürmeyecek dozlarda da rastlanır.

Sonuç olarak söylemek mümkünki, fiziolojik yönden yeniden canlanacak substandard mubadele (veya hipometabolik mubadelenini canlılık siniri) belirtiler değişik görünüşteki intoksikasyon (zehirlenme) larda, hayvanların standard mubadele derecesinden 2 kat aşağıdadır, yeniden canlanmayacak substandart mubadete (vega letal (öldürecek) hipomeabolik değişim (mubadele) siniri) ise 3 kat aşğıdadır.

Anahtar Sözcükler: Oksijen-gaz metabolizması, Yılan zehiri, zehirlenme, *Mus*

Introduction

Gas-oxygen metabolism studied in optimal conditions for organisms is usually determined as basal metabolism (mainly for humans) or as the standard metabolism (mainly for small animals) [14]. These forms of metabolism are considered minimal metabolisms for organisms [2], although this question is disputable [1-3].

It is known that the metabolic intensity may vary according to the organism's physical and metabolic loading [1-4] and that decreases during hypometabolic states conditioned by hypoxia, hypothermia and other factors [1-4]. Analysis of the literature shows that the nature of the hypometabolic state of the organism is not well known. The physiological range of substandard metabolic alteration is unknown, as are its reversible and irreversible limits. We think that the problem is directly connected with the organism's life-tolerance to different factors inluding toxic chemicals.

The aim of the present study is to examine the substandrad metabolism in mice under the effects of lethal and nonlethal (half-lethal) doses of Vipera lebetina venom and of some hypometabolic agents.

Methods and materials

White mice 25-30 g in weight were used in the experiments. They were placed in a hermetic chamber for the study of gas-oxygen metabolism. The intensity of oxygen consumption by the animals is determined by polarographic method with Clark's oxygen electrode. Atmosphere gas in the chamber was stirred by micropump. The oxygen content in the 100-ml chamber used was 20 ml (20%).

The control group was studied by intrabdominal injection of 0.9% NaCl solution.

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Experimental groups were injected with lethal and nonlethal doses (as much as twofold lower than the lethal dose) of the venom of *Vipera lebetina* [5] and the hypometabolic agents: aminooxyacetate [6], catacin [7], halothane [9] and serotonin [9]. These substances were dissolved in 0.9% NaCl solution before experiments.

Results and Disscusion

Table 1 shows the effect of lethal and nonlethal doses of different agents on the gas-oxygen metabolism of the mice. The data indicate that all the agents used decreased oxygen consumption by animals.

The gas-oxygen metabolism level decreased by 55% upon aminooxycetate and catacin and by 43-50% upon snake toxin, serotonin and halothane effects (Fig. 1). It can be seen that the difference between the agents used reached 10-15% in decrease of the metabolic potency.

In should be mentioned that the agents used in the present experiment differ considerable in their mechanisms of action. Snake toxin includes many hydrolytic enzymes and causes hemolysis and cell necrosis [5]; aminoxyacetate blocks the aminotransferase enzymes [6]; catacin is antihypoxant and decreases metabolic activity and mitochondrial respiration by inhibition at the respiratory chain (7); anesthetic halothane inhibits the mitochondrial respiration at NAD-dehydrogenase level [8] and is used in medicine; the serotonin level rises in the hibernating animals and is thought to be responsible for the decrease in their metabolic activity [9].

According to our data, the agents all had similar effects on animal oxygen consumption. It is very likely that the parameter of oxygen consumption reflects nonspecific the energetic state of the organism during its intoxication.

As seen in Fig. 1 the administration of lethal doses of the drugs led to decreases of 60 to 75% in the animal oxygen consumption when compared with the control levels. This is an approximately threefold decrease in the standard metabolic rate. On the other hand, independently of the nature of the drug, the intensity of the gas-oxygen consumption in mice decreased approximately twofold during nonlethal intoxication. It is thus clear that agents of different nature possess aproximately the same effects on the organisms energy metabolism.

The results of the usage of lethal and nonlethal doses of different substances on the gas-oxygen consumption of the organism indicate the following peculiarity of the

Agents administered to mice	Nonlethal doses		Lethal doses	
	doses of agents	Oxygen consumption ml/kg.h	doses of agents	Oxygen consumption ml/kg.h
control 0.9% NaCl	-	4271.3+216.8	-	4271.3-216.8
snake venom	1 mg/kg	2472.5+193.3	2 mg/kg	1637.5+142.6
catacin	300 mg/kg	2121.6+216.3	600 mg/kg	1373.3+152.1
halothane	5 mM	2420.9+157.2	10 mM	1388.9+122.1
serotonin	60 mg/kg	2381.6+148.3	120 mg/kg	1471.9+108.3
aminooxyacetate	0.3 mM	2135.5+166.7	1 mM	1494.9+132.3

Table 1. Influence of different agents on gas-oxygen metabolisms of mice (n=12-18)

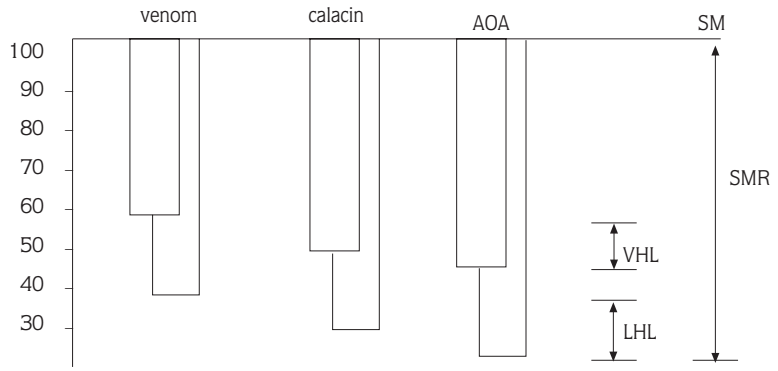

Figure 1. Degree of the gas-oxygen metabolic decrease in mice after intraabdominal injection of Vipera lebetina venom, catacin and aminooxyacetate (AOA). Standard metabolism of control animals: 100%. Doses of agents used are indicated in Table 1. Abbreviations: SM: standard metabolism, SMR: subbasal metabolic range, VHL: vital hypometabolic limit, LHL: lethal hypometabolic limit.

substandard metabolism. The substandard metabolic level is approximately twice as low as the standard metabolic one when nonlethal dose of a drug is administered. The substandard metabolic alteration may be called the vital metabolic range because the organism maintains its vitality within this range of metabolic activity. The lower level of this metabolic range shows the lower limit of the vital metabolic potentiality of an organism.

Lethal doses of the tested substances decrease the organism gas-oxygen consumption approximately threefold. This alteration of the metabolic rate is called a lethal hypometabolic range since the organism does not maintain its vitality under this condition. The lower level of this metabolic range shows the lethal limit of the organism metabolic state.

Fig. 2 shows the vital hypometabolic limit and lethal hypometabolic limis as components of the subbasal (substandard) metabolism.

Thus, data obtained characterize the substandard metabolism and its parameters under the effects of different intoxications on the animal organism.

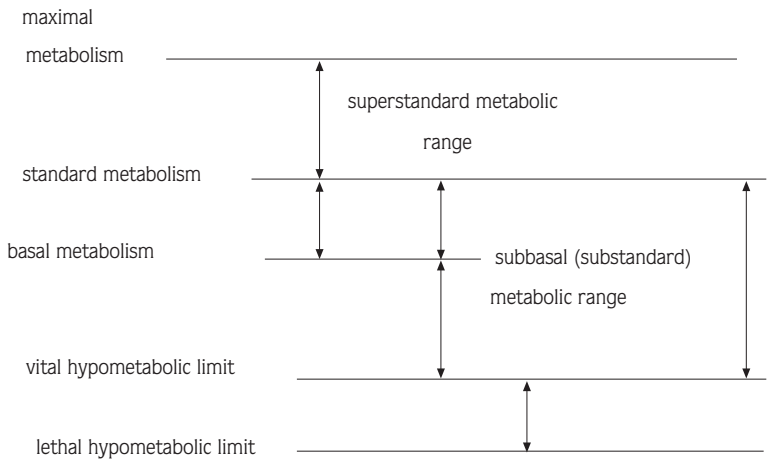

Figure 2. Different form of metabolism and metabolic ranges of organism in its different states. Maximal metabolism is the active metabolic status of an organism during physical and functional loading. Superstandard metabolic range is the energetic reserve that is placed over the standard (basal) metabolic level. Basal metabolism is characterized metabolism in total resting of large organisms (mainly of human). Standard metabolism is usually determined in small rodents under standard conditions during its common activity. Vital hypometabolic limit is the hypometabolic level that is reversible for organism vitality. Lethal hypometabolic limit is the metabolic level that is irreversible for the organism vitality.

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