INCREASING THE RESISTANCE OF ANIMALS TO DECOMPRESSION SICKNESS BY PREPARATION OF BILE ACIDS

Ya. V. Ganitkevich

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Preliminary intraperitoneal injection of sodium cholate and desoxycholate (2 mg/100 g body weight) into mice delays and alleviates the course of decompression sickness and reduces the mortality. Injection of the same compounds into the blood stream of rabbits (6-20 mg/kg) alleviates the manifestations of decompression sickness.

Resistance to decompression sickness (DS) is determined by the state of reflex mechanisms forming responses of the vascular and respiratory systems to air embolism [11], and the central component of DS [10]. Previously the author has demonstrated a marked increase in the resistance of rabbits to experimental air embolism following administration of bile acids. The action of these compounds was accordingly studied in DS.

EXPERIMENTAL METHOD

Experiments were carried out on 222 mice and 10 rabbits. DS was produced in the mice and LD_{50} calculated. For this purpose the air pressure inside a pressure chamber* containing the animals was raised for 40 sec up to 12 atm, exposure lasting for 15 min. Decompression was carried out for 25 sec. The experimental group of animals received an intraperitoneal injection of 0.2% sodium cholate or desoxycholate in a dose of 2 mg/100 g body weight, made up in physiological saline, 30-50 min before decompression. Control animals received the same volume of physiological saline.

Resistance of the rabbits to DS was studied by a method similar to that of determination of the "non-decompression time." The air pressure in the chamber was raised for 2 min to 7 atm. The exposure to this raised pressure lasted for 9-12 min. Decompression was carried out for 3 min. Depending on the duration of exposure to the raised pressure and on individual sensitivity of the animals, various forms of DS were observed among the rabbits: mild, moderately severe, and severe. Bile acids (15-20 mg/kg sodium cholate or 6-10 mg/kg sodium desoxycholate) were injected into the rabbits as a 1-2% solution into the marginal vein of the ear 30-50 min before decompression. Experiments with injection of bile acids alternated with control experiments. The total number of experiments was 58.

EXPERIMENTAL RESULTS

Preliminary injection of bile acids reduced the incidence of DS in the mice and, in particular, the mortality (Table 1).

*The investigations were carried out in the barolaboratory of the department of underwater swimming and life-saving service of the S. M. Kirov Military Medical Academy.

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TABLE 1. Effect of Injection of Bile Acids on Decompression Sickness in Mice

Group of animals	Number of animals in group	developing disease: total	of which: total	of which: died	of which: remainder with disturbances	of which: recovered	remained free from disturbances: total	including: not developing	including: recovery
Experimental	111	53(48)	47(42)	2(1,8)		4(3,6)	62(56)	58(52)	4(3,6)
Control	111	66(60)	63(57)	2(1,8)		1(0,9)	46(41)	45(40)	1(0,9)
Difference		−13	−16	—		+3	+16	+13	+3
		(−12)	(−15)			(+2,7)	(+15)	(+12)	(+2,7)
χ^2		3,1	4,6			1,3	5,2	3,1	1,3
P		>0,05	<0,05			>0,1	<0,05	>0,05	>0,1

*Figures in parentheses show percentages relative to total number of animals in group. All data given referred to state over a period of 24 h.

TABLE 2. Changes in Dynamics of Decompression Sickness in Mice Under the Influence of Bile Acids

Time from end of decompression (in min)	Number of animals: experimental group: total	experimental group: dying	experimental group: no disturbances	control group: total	control group: dying	control group: no disturbances
0—5	31	27	80	41	34	70
6—10	13	9	67	19	15	51
11—30	7	6	60	2	5	49
31—60	1	0	61	2	0	47
1—24 h	1	5	62	2	9	46
Total	53	47	62	66	63	46

In the experimental group the number of animals developing the disease and, in particular, the number dying were reduced, while the number of animals remaining without disturbances after decompression was sharply increased. Some animals of the experimental group which developed the disease recovered, whereas control animals which developed DS as a rule died toward the end of the day. In a few animals the motor disturbances persisted for several days. Under the influence of bile acids the dynamics of development of DS were modified, as a rule taking place more slowly (Table 2).

In experiments on rabbits an increase in the time of exposure to a raised pressure in the repeated control tests led to the development of more severe DS. Whereas in the first control experiment DS did not develop, an increase of 0.5 min in the exposure led to the development of mild DS, and an increase of 1 min to moderately severe DS. Repetition of the test with the same exposure revealed rather less marked motor disturbances, but the increase in respiration rate was usually greater and more prolonged.

Injection of bile acids after an exposure of the same length as in the preceding control test led to considerable alleviation of the manifestations of DS. An increase in exposure by 0.5-1 min after injection of bile acids (10 experiments) led to alleviation of the manifestations of DS in half of the cases, changes were absent in two experiments, and only in three experiments was the disease more severely manifested (one of these rabbits received a reduced dose of cholic acid). In one experiment in which sodium desoxycholate was injected, an increase in exposure by 2 min did not increase the severity of the DS. In repeated control tests with an exposure equal to that of the preceding experiment, no decrease in the severity of the disease was observed, but as a rule the manifestations of DS were more marked.

In animals receiving several preliminary injections of bile acids, the course of DS was milder in the repeated control tests. Repetition of some control tests did not produce such marked changes. This suggests that injection of bile acids has a long after-effect and accelerates adaptation of the animals to DS. In experiments with administration of bile acids, the maximal respiration rate was much lower than in control tests, especially in a severe form of the disease (135 ± 6 and 177 ± 7 breaths/min respectively); the duration of dyspnea also was reduced.

Concerning the mechanism of action of bile acids it can be postulated that, with their marked neurotropic action [5, 6, 8, 9], they diminish the reactions of the nervous system due to decompression air embolism, as a result of which the disease follows a milder course. Support for this hypothesis is given by the fact that dyspnea was reduced in the animals developing the disease, and responses of the cardiovascular system were improved following administration of bile acids in the air embolism experiments. Changes

in these responses of the animal lie at the basis of increased resistance to DS in trained animals [12]. Bile acids evidently diminish reflexes from vascular interoceptors, as a result of which the reflex spasm of the blood vessels is reduced and this, in turn, facilitates the propulsion of gas bubbles and reduces the risk of occlusion of the vessels by emboli.

At the same time, allowance must be made for the effect of bile acids on the physicochemical properties of the blood and body tissues. Injection of bile acids into animals may reduce the surface tension of the body fluids and tissue extracts [7], while according to theoretical calculations [3], the magnitude of the surface tension must play a role in the formation and conversion of gas bubbles in the blood. The character and behavior of gas bubbles in a liquid depend on the surface tension [13, 14]. Surface-active substances affect the velocity of movement of oxygen bubbles in a liquid, help to form smaller bubbles, and increase the rate of solution of oxygen [16]. Synthetic surface-active substances can minimize manifestations of air embolism [12] and reduce the mortality among rats from DS [14]. Evidently a definite role in the mechanism of action of bile acids is played by their high surface activity, their ability to be adsorbed on a phase boundary, and their ability to form unimolecular layers with specific mechanical, diffusion, and other properties.

The possibility is not ruled out that preliminary administration of bile acids may influence the process of saturation of the body tissues with gases, which depends on the state of the respiratory and cardiovascular systems [1, 4].

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