INFLUENCE OF SODIUM AMYTAL ON SUGAR SECRETION BY THE LIVER AND ITS EXTRACTION FROM THE BLOOD BY CERTAIN TISSUES

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The literature data on the influence of sodium amytal on the sugar content in the blood are contradictory. Some authors [4] have found considerable hyperglycemia under the influence of large doses of barbiturates; others [7], on the contrary, have found hypoglycemia, while still others [8-10] could not detect any changes in the sugar content of the blood after single or repeated introduction of sodium amytal [12].

We showed earlier [2] that glycemia in dogs, even under profound amytal narcosis, lasting for 24 h, is only slightly reduced, and that, evidently, in connection with prolonged starvation.

It is known [11], that a single introduction of sodium amytal (0.3 g) does not influence the carbohydrate metabolism in the muscles of hypertension patients, while the systematic administration of sodium amytal in sleep therapy (course of treatment two 5-6 day cycles with a daily dose of 0.6-0.8 g) leads to a reduction of the carbohydrate assimilation by the tissues. The same is also observed in amytal intoxication.

TABLE 1. Passage of Blood Sugar into the Tissues of the Hind Legs and its Secretion by the Liver into the Blood in the Healthy Dog Fiska during Profound Amytal Narcosis (in mg%)

Index studied	Time of investigation (in hours)																
	1/6	1/3	1	2	3	4	5	5.5	6	6.5	7	7.5	8	9	9.5	10	Average
Sugar content in the arterial blood	82	83	79	79	80	72	70	70	70	70	68	68	63	63	68	63	72
Passage of sugar into the tissues of the hind legs	3	7	4	7	4	0	3	4	4	4	4	5	7	2	9	0	3.8
Passage of sugar into the organs of the portal system	6	9	5	7	5	0	4	5	11	11	5	16	7	6	11	8	7.3
Secretion of sugar by the liver	10	10	14	13	9	12	7	13	16	17	16	20	7	7	8	23	12.6

Barbiturates exert little influence on the sugar consumption by the muscles and its secretion by the liver in dogs in a state of profound narcosis [5].

In our previous work [2] it was established that during a period of profound amytal narcosis, over periods of 13 and 24 h, the blood sugar passes into the tissues of the hind legs and the brain, almost the same as in normal, awake dogs. If the respiration rate was greatly slowed and the temperature reduced under the influence of sodium amytal, the extraction of sugar by the tissues was more or less sharply decreased.

In this investigation we attempted to determine how the passage of blood sugar into the organs of the portal

TABLE 2. Passage of Sugar into the Tissues in Healthy Dog during a Period of Profound Amytal Narcosis (Average Data)

Period of experiment	Belka				Sapsan				Fiska				Novaya			
	No. of investigations	Sugar level in the arteries	Passage of sugar		No. of investigations	Sugar level in the arteries	Passage of sugar		No. of investigations	Sugar level in the arteries	Passage of sugar		No. of investigations	Sugar level in the arteries	Passage of sugar	
			Into tissues of hind legs	Into organs of portal system			Into tissues of hind legs	Into organs of portal system			Into tissues of hind legs	Into organs of portal system			Into tissues of hind legs	Into organs of portal system
		In mg%				In mg%				In mg%				In mg%		
First	6	77	3.7	3.5	5	75	4.6	7.0	8	77	3.2	5.0	6	83	4.5	9.3
Second	5	78	9.0	8.6	7	66	6.7	13.0	8	66	4.4	9.4	6	83	14.0	17.0

TABLE 3. Secretion of Sugar into the Blood by the Livers of Healthy Dogs in a Period of Prolonged Profound Amytal Narcosis (Average Data)

Period of experiment	Belka			Sapsan			Fiska			Novaya		
	No. of investigations	Sugar level in the portal vein	Amt. of sugar secreted by the liver	No. of investigations	Sugar level in the portal vein	Amt. of sugar secreted by the liver	No. of investigations	Sugar level in the portal vein	Amt. of sugar secreted by the liver	No. of investigations	Sugar level in the portal vein	Amt. of sugar secreted by the liver
		In mg%			In mg%			In mg%			In mg%	
First	6	74	7.7	5	68	8.3	8	72	11	6	73	9
Second	5	69	9.6	7	53	18	8	57	14	6	65	18.7

TABLE 4. Glycogen Content in the Livers of Dogs during a Period of Prolonged Profound Amytal Narcosis

Time of determination	Glycogen content (in mg% of glucose)			
	Belka	Sapsan	Fiska	Novaya
11 h	6080	1100	1490	3570
12 h 30 min	3030	1100	980	2450
15 h	3890	615	560	1300
16 h 30 min	1680	375	350	340
18 h			350	
19 h 30 min			280	

system is changed in comparison with the tissues of the hind legs during prolonged narcosis induced by sodium amytal.

EXPERIMENTAL PROCEDURE

The procedure and setup of the experiments did not differ from those described earlier [2]. The blood for the sugar determination was taken simultaneously from the renal, portal, and femoral veins, as well as from the femoral artery.

EXPERIMENTAL RESULTS

From Table 1 we can see that in the dog Fiska, glycemia was gradually reduced over a period of 10 h of profound amytal narcosis. This was evidently due to 30 h starvation (20 h before the experiment). A similar decrease in glycemia was detected in the dog Sapsan. In the rest of the animals in the second half of the experiment, which lasted for 7-7.5 h, glycemia was not reduced (Table 2).

The passage of blood sugar into the tissues of the hind legs in Fiska was an average of 3.8 mg%. In the control dogs, this index was higher—4.8 mg%. Such a difference is probably explained by the lower average blood sugar level in the narcotized dog—72 mg%, in comparison with that in the awake dog—95mg% [1]. More sugar passed into the tissues of the hind legs in the dogs Sapsan, Belka, and Novaya as well, in spite of the fact that glycemia remained in normal limits for Belka and Novaya during the entire experiment, and in Sapsan it was even somewhat reduced.

In Belka, the passage of sugar into the organs of the portal system was similar to the transfer of sugar to the tissues of the hind legs, while in the other 3 dogs, the 1st index was considerably higher (see Table 2). Noteworthy is the fact that during the 2nd half of the experiment, more sugar passes into the tissues of the hind legs than organs of the portal system than in the 1st half of the experiment.

Sugar was secreted by the liver for 13 h in Fiska. The same was also noted in the other dogs (Table 3). During the period of profound amytal narcosis, the liver secreted almost the same amount of sugar into the blood as the liver of angiostomized awake dogs (15 mg%) [1]. Moreover, during the period of profound amytal narcosis, the liver does not lose its homeostatic influence and secretes sugar into the blood corresponding to the inflowing amount.

The glycogen content in the liver is greatly reduced during the entire extent of prolonged amytal narcosis (Table 4). However, we do not have at our disposal data that would permit us to judge the degree to which such a reduction is due to starvation of the animals and that to which it is due to the influence of sodium amytal.

Sodium amytal weakens the utilization of oxygen by the tissues [13], but, as has been shown earlier [2], as well as in this work, the passage of sugar into the tissues of the hind legs, brain, and organs of the portal system is not reduced during the entire period of prolonged profound amytal narcosis, in comparison with that in the awake animals. It is only slightly reduced during the first half of the experiment, but then is appreciably increased in the 2nd. Such an extraction of blood sugar over a period of 7-24 h gives evidence that it is utilized by the tissues.

If this did not occur, then the passage of sugar into the tissues of the hind legs and organs of the portal system would become even smaller on account of its increased accumulation. Actually, in the 2nd half of the experiment it even increased, which is evidently due not to its intensified utilization during profound amytal narcosis but to somewhat decelerated blood circulation. In favor of the latter hypothesis is the evidence of an increase in the passage of sugar into the tissues during the 2nd half of the experiment, even in the presence of a reduced blood sugar level (see Table 2, dogs Sapsan and Fiska).

The normal organism of the healthy dog, 10 kg in weight, utilizes 0.19 g of sugar per kg of weight per h [14]. If we proceed from this calculation, then Fiska, who weighed 13 kg, consumed approximately 26 g of glucose in 10 h. Her liver contained approximately 5 g of glycogen. Consequently, more than 20 g of glucose was secreted by the liver at the expense of newly formed glucose. Similar calculations show that the livers of the other dogs also secrete a substantial amount of glucose not formed from the hepatic glycogen during prolonged amytal narcosis. Consequently, amytal narcosis, even prolonged, does not stop the process of glucose formation from the liver glycogen, from the lactic acid that flows into it, as well as from other products.

Since the mobilization of fats, amino acids, and lactic acids formed from the muscle glycogen in the liver is related to the functions of the sympathetic nerves and the adrenocorticotropic function of the anterior lobe of the pituitary, on the one hand, and of the brain and cortical portion of the adrenals, on the other, we might assume that the mechanisms of glycogenogenesis during amytal narcosis remain the same, although they are decelerated.

The liver does not lose its homeostatic properties—an increase in the secretion of sugar into the blood upon reduced influx to it, while the tissues extract less sugar from the blood when less of it flows into them.

All this gives evidence of a conservation of more or less normal metabolism during prolonged amytal narcosis, both in the liver and in the tissues of the hind legs and organs of the portal system.

SUMMARY

In profound amytal anesthesia lasting 7 - 24 h glycemia in dogs either remained unchanged or dropped slightly, while the passage of blood sugar into the tissues of the posterior extremities and organs of the portal system proved to be the same as that in the wideawake animals.

During profound amytal anesthesia the liver secreted about the same amount of sugar into the blood as did the liver of angiostomized wideawake dogs. At the same time,the liver did not lose its homeostatic property, viz., that to increase the sugar secretion into the blood under conditions of the reduced sugar supply, whereas the tissues did not lose their property to extract less sugar from the blood when the sugar supply was reduced.

The above findings show that during prolonged amytal anesthesia more or less normal metabolism is retained both in the liver and in the tissues of the posterior extremities and the portal system organs.

LITERATURE CITED

1. S. G. Genes. Pathogenesis and Therapy of Sugar Diabetes [in Russian]. Khar'kov-Kiev (1944).
2. S. G. Genes and P. M. Charnaya. Byull. Éksper. Biol. (1960), No. 1, p. 54.
3. S. G. Genes, N. S. Veller, and P. M. Charnaya. Pat. Fiziol. (1960), No. 6, p. 34.
4. V. N. Georgadze. Farmakol. i Toksikol. (1950), No. 5, p. 22.
5. I. A. Lerman. In book: Collection of Scientific Transactions of Bashkir Medical Institute [in Russian]. Ufa (1938), Vol. 1, p. 187.
6. L. M. Makarevich-Gal'perin and S. N. Ushenko. Probl. Éndokrinol. (1957), No. 4, p. 16.
7. V. S. Men'shikov. Transactions of the Central Institute of Psychiatry [in Russian]. Moscow (1941), Vol. 2, p. 392.
8. G. F. Milyushkevich. In book: Mechanisms of Pathological Reactions [in Russian]. Leningrad (1949), No. 11-15, p. 87.
9. O. A. Naletova. Summaries of Reports at the Expanded Session of the Scientific Council, Institute of Physiology, Academy of Medical Sciences, USSR, Held Jointly with the Scientific Councils of the Institutes of Pharmacology, Neuropathology, Surgery, Pediatrics, and Experimental Medicine, Academy of Medical Sciences, USSR, Devoted to the Problems of the Experimental Substantiation of Sleep Therapy [in Russian]. Moscow (1954), p. 45.
10. Yu. A. Povorinskii. Zh. Nevropatol. i Psikhiatr. (1955), No. 1, p. 6.
11. R. M. Ptukha. In book: Problems of the Pathology of the Cardiovascular System [in Russian]. Kiev (1959), p. 233.
12. A. E. Troshina. Influence of Prolonged Use of Barbamil on the Carbohydrate Metabolism and Biocurrents of the Brain. Author's Abstract of Candidate's Dissertation [in Russian]. Ryazan' (1956).
13. L. S. Goodman and A. Gilman. The Pharmacological Basis of Therapeutics. New York (1956), p. 126.
14. W. M. Yater, J. Markowitz, and R. F. Cahoon. Arch. intern. med. (1933), v. 51, p. 800.

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
