THE EFFECT OF SODIUM AMYTAL ON THE PASSAGE OF SUGAR FROM ARTERIAL BLOOD INTO TISSUES OF THE HIND LIMB AND BRAIN

C. G. Genes and P. M. Charnaya

Department of Pathophysiology (Head – Honored Scientist Professor C. G. Genes) Ukranian Institute of Experimental Endocrinology (Director – Senior Scientific Collaborator S. V. Maksimov)

(Presented by Active Member AMN SSSR V. N. Chernigovskii)

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It is known that certain doses of anesthetic produce histological anoxia and reduce oxygen utilization [2]. Ether [10], Sodium amytal, and other substances also possess this property [14].

A consequence of the reduced oxygen utilization by the tissues is that the breakdown of glucose is also reduced. Some authors [1] have attributed the hyperglycemia which occurs under ether anesthesia to reduced oxygen utilization, although this also occurs under sodium amytal without any increase in blood sugar level [12].

If anesthetics reduce carbohydrate and oxygen utilization by the tissues, then it would be expected that there would also be reduced passage of sugar from arterial blood into the tissues.

We have studied this problem in dogs and have found to what extent sodium amytal influences the amount of sugar passing from the blood into the tissues of the hind limb (as constituting the principal mass of tissue) and brain, where utilization of the blood glucose is of special importance [5, 6, 16, 17].

METHOD

The experiments were carried out on healthy dogs under deep sodium amytal anesthesia. Repeated injections of a 2.5% solution of sodium amytal were given: the first injection was given subcutaneously, the remainder intravenously as required.

As an example, a dog weighing 24 kg received sodium amytal injections as follows: at 8 a.m. – 50 mg/kg; at 8:30 a.m. – 6 mg/kg; at 8:40 a.m. – 4 mg/kg; at 9 a.m. – 3 mg/kg; at 10 a.m. – 3 mg/kg; at 11:10 a.m. – 6 mg/kg; at 12:30 p.m. – 3 mg/kg; at 2 p.m. – 3 mg/kg; at 3:20 p.m. – 3 mg/kg, and at 7:20 p.m. – 2 mg/kg. When the animals were deeply anesthetized, and the corneal reflex could no longer be obtained, an opening in the skull in the region of the superior longitudinal sinus was cut by means of a trepine; the femoral artery and vein were exposed, a laparotomy was performed and the caudal portion of the pancreas removed; these dogs served as controls for the remaining experiments. The blood sugar level was determined using the method of Hagedorn-Jensen: This was done three times every 5 minutes before, and once hourly for 12-13 hours after laparotomy. Blood for examination was taken simultaneously from the femoral artery and from the superior sagital sinus. The normal body temperature was maintained by wrapping the animal up in blankets and warming with an electric lamp.

RESULTS

The Effect of Sodium Amytal on the Passage of Sugar into the Tissues of the Hind Limbs (Table 1)

A prolonged deep anesthesia induced by injecting sodium amytal 7-10 times over a period of 13 hours caused no change in the blood sugar level. The level fell only from 93-108 mg% at the beginning of the experiment to 80-85 mg% at the end, and this change could be ascribed to the 33 hours fast (the animals fasted for 20 hours before the experiment).

The passage of the sugar from the arterial blood into the tissues of the hind limb varied during the experiments over quite wide limits, and had an average value of 6 mg%. The transfer coefficient, which represents the ratio of the level in the tissue fluid to that in the blood, had a value of 7% in dog No. 8 and 6.6% in dog No. 9. In three determinations of the arteriovenous difference in blood sugar level in 6 dogs under deep sodium amytal anesthesia, the average tissue fluid concentration was 5.4 mg%, the blood sugar 86 mg%, giving a transfer coefficient of 6.3%.

These results differ little from those we obtained [5, 6] in healthy active dogs where the tissue sugar was 4.7 mg% and the transfer coefficient 5%.

TABLE 1 Blood Sugar Level and Amount (in mg%) Passing into Tissue in Animal Under Sodium Amytal Anesthesia

Before operation, min			After operation, hour														
0	5	10	1	2	3	4	5	6	7	8	9	10	11	12	12½	13	13½
			Dog No. 8. Blood sugar level (artery)														
93	92	91	92	91	89	84	79	84	88	90	91	78	88	79	82	80	
			Passage of sugar into brain														
11	17	15	22	15	22	22	15	13	9	20	20	26	24	16	18	14	
			Passage of sugar into tissues of hind limbs														
6	10	9	7	7	4	+1	5	6	8	16	+2	8	+1	11	3		
			Dog No. 9. Blood sugar level (artery)														
108	110	108	101	91	90	77	83	83	85	88	88	90	88	90	—	88	85
			Passage of sugar into brain														
19	16	18	11	12	11	11	16	15	17	20	20	18	14	14	—	22	17
			Passage of sugar into tissues of hind limbs														
0	6	2	5	5	9	1	17	4	5	6	10	2	2	13	—	11	9

It was quite otherwise with dogs under deep ether anesthesia [3-5, 7-9]. The tissues of the hind limbs in these animals removed 11 mg% sugar from arterial blood. We require to know the cause of this difference. Unlike sodium amytal, ether considerably increases the blood sugar level (from 126 to 141 mg%), and the higher its concentration the greater the amount of glucose extracted by the tissues. The considerable increase in the passage of sugar from the arterial blood into the tissues of the hind limbs does not however contradict the view that ether reduces the utilization of glucose by the tissues. In order to form a correct estimate of the amount of blood sugar transferred to the tissues, it is necessary to compare normal conscious animals with those under ether anesthesia when both have the same blood sugar level. We found that in the waking state [3-8], increasing the blood sugar to 129 and to 152 mg% by injection caused the transfer into the tissues of the hind limb to reach values of 14 and 21 mg%, i.e., values which are higher than under ether anesthesia. The greater transfer of sugar to the hind-limb tissues in waking animals as compared with those under ether anesthesia when both have the same blood sugar level is shown by the fact that in the first group the transfer coefficients were 10.9 and 13.8 and in the second 7.1 and 8.7.

Thus ether reduces the passage of sugar into the tissues of the hind limbs, but does not suppress it entirely. Sodium amytal, however, administered over a period of 13 hours changes neither the blood sugar level nor the absolute nor the relative amount passing into the hind limb tissues. We obtained these results in dogs in which sodium amytal exerted no toxic effect. During the whole of the experiment the respiration, pulse rate and rectal temperature remained normal. Different results were obtained in animals to which sodium amytal was toxic: The pulse rate fell from 106 to 80 per minute, respiration from 12 to 5 per minute, and the rectal temperature from 39 to 28° (Table 2).

In dogs No. 5 and 6, the passage of sugar into the tissues of the hind limbs was less than in Nos. 8 and 9, the values being 4.3 and 2.8 mg%. The transfer coefficients were 5.1% for No. 6, and 3.3% for No. 5. In view of the fact that in both dogs the blood sugar level was normal (86 and 82 mg%), this reduced transfer coefficient indicates a reduced ability of the tissues to utilize blood sugar.

In one dog, the passage of sugar into the limb tissues was measured hourly for 24 hours with the animal under deep amytal anesthesia. During this period the rectal temperature remained normal at 38-39°, the respiration remained within normal limits being 22 at

the beginning and 16 per minute at the end; the pulse rate was 120-144 per minute. The blood sugar level in this dog at the end of the experiment was the same as at the start, the average value of 23 determinations being 83 mg%. However the passage of sugar into the tissues varied considerably; it had an average value of 2.5 mg% and a transfer coefficient of 3%. In this animal, judging from the reduced passage of sugar into the brain over a 4-hour period (see Table 2), sodium amytal had a somewhat toxic effect, which was not reflected in the rectal temperature or respiration, though it did affect the utilization of sugar by the tissues.

It can be seen therefore that sodium amytal given in doses sufficient to cause anesthesia but which do not cause any toxic effects does not interfere with the maintenance of a normal blood sugar level or with the normal transfer of sugar into the tissues; however when given in toxic doses the blood sugar level is not changed, but there is less transfer into the tissues of the limbs which represent the main tissue mass of the body.

Sodium amytal and the transfer of sugar into the brain (Tables 1, 2). The brain utilizes glucose almost exclusively [16, 17] and more intensely than do other tissues. Thus, the transfer of sugar from the blood to the kidneys in a healthy dog represents 1.8 mg%, into the intestinal wall – 3 mg%, into the muscle of the heart – 3.9 mg%, into the spleen – 4 mg%, into the limb tissues – 4.7 mg%, and into the brain – 8 mg% [5, 6]. The higher the arterial blood sugar level, the greater the amount of sugar passing into the brain [11, 12]. The extraction and utilization of blood oxygen by the brain also increases parallel with the passage of sugar into it [15]. The requirement of the brain for sugar and oxygen is reduced in human subjects when in a drug-induced sleep [13]. It has been shown in in vitro experiments that barbiturates applied to brain tissue reduce oxygen utilization. When glucose is added to the brain tissue, there is also an increase in the uptake by it of atmospheric oxygen. In the case of the intact animal, different results are obtained. The transference of sugar into the brain from arterial blood during amytal anesthesia is considerably more rapid than in the waking state.

As the results of Table 1 show, over a 13-hour period the transfer of sugar to the brain in dog No. 8 varied from 9 to 26 mg%, but in dog No. 9 from 11 to 22 mg%. The average extraction of sugar by the brain in both dogs was nearly the same – 17 and 16 mg%, but the transfer coefficient (which is also coefficient of utilization) was 18% in dog No. 9 and 20% in dog No. 8. This rapid

TABLE 2 Blood Sugar Level and Its Passage (in mg %) into the Tissues, Sodium Amytal Anesthesia

Before operation, min			After operation, hour													
0	5	10	1	2	3	4	5	6	7	8	9	10	11	12	13	13½
			Dog No. 5. Blood sugar level (artery)													
89	93	89	94	87	83	76	83	81	81	85	89	80	87	85	85	86
			Passage of sugar into brain													
20	20	14	9	13	12	12	12	9	5	7	12	4	4	4	0	0
			Passage of sugar into tissues of hind limbs													
+2	0	15	+4	11	7	+9	+2	5	1	4	6	4	6	2	3	0
			Dog No. 6. Blood sugar level (artery)													
94	96	83	87	82	70	78	76	75	74	74	82	81	83	90	92	
			Passage of sugar into brain													
20	18	11	15	17	0	11	11	14	0	4	+1	+2	0	0	0	
			Passage of sugar into tissues of hind limbs													
5	15	10	11	2	+4	1	2	10	7	4	1	+2	9	0	+2	

transfer of sugar to the brain also occurred in 7 healthy dogs during deep amytal anesthesia. The extraction of sugar from the blood by the brain in these dogs had an average value as determined from 21 measurements of 17 mg%, and the utilization coefficient was 20%.

In one healthy animal the transfer of sugar into the brain was studied hourly for 24 hours in an animal under deep amytal anesthesia. In spite of the fact that in one dog for a 4-hour period toxic symptons occurred which led to a marked fall in the transfer of sugar to the brain (4, 5, 1, 5 mg%) the average value was nevertheless 12 mg%, and the utilization coefficient 14.5%.

Thus with amytal anesthesia, sugar utilization by the brain remains at a high level for as long as 24 hours. It must be noted that even in the last hours of the experiment the brain continues to extract the same amount of sugar from the blood as at the start of the experiment. This was found not only during the 13-hour but also during the 24-hour experiment. Therefore deep amytal anesthesia does not affect the power of the brain to utilize blood sugar rapidly. These results were obtained in dogs on which sodium amytal had no toxic effect. If in any animal there was a fall in respiration rate or in body temperature, then the extraction of sugar by the brain was also reduced (see Table 2). From the results given in Table 2 it can be seen that in dogs Nos. 5 and 6 the transfer of sugar to the brain is greatly reduced, and may even cease entirely in the last 7 hours of the experiment. This affects the average value of the sugar transferred to the brain during a 13-hour period: 0.2 mg% in dog No. 5 and 7.4 mg% in dog No. 6 with coefficients of utilization of 11 and 9%, respectively.

Consequently, when amytal produces no toxic effects, the brain maintains its ability to extract sugar rapidly from the blood. However if amytal exerts a toxic influence on the body, then this function of the brain is markedly reduced, and may fail entirely.

SUMMARY

The transfer of sugar from the blood into the limb tissues was shown to increase when either of two anesthetics was administered; this was due to a raised blood sugar level. When the blood sugar level rises, its transfer into the limb tissues is more marked in healthy nonanesthetized animals than in those under ether; it is also greater in animals under ether anesthesia from whom the pancreas has been removed than in similarly operated nonanesthetized dogs. Prolonged amytal anesthesia has no effect on the blood sugar level or on its normal transfer into the limb tissues. In the case of toxic symptoms which include a reduced rate of respiration and a lowered rectal temperature and which result from amytal anesthesia, the transfer of sugar into the limb tissues is reduced. Prolonged amytal anesthesia not only does not prevent the extraction of sugar from the blood by the brain but even increases it (in comparison with the amount of sugar transferred to the brain of nonanesthetized animals). In animals, sugar extraction by the brain is markedly decreased or completely arrested during the toxic action of sodium amytal.

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