THE EFFECT OF A NEUROLYTIC MIXTURE ON CERTAIN BIOCHEMICAL BLOOD INDICES IN TRAUMATIC AND ANAPHYLACTIC SHOCK

M. A. Slastikhin and G. A. Kataeva (Leningrad)

(Received December 10, 1958. Presented by Active Member AMN SSSR V. N. Chernigovskii)

In the prophylaxis and treatment of traumatic shock extensive use has been made recently of various chemical substances with diversity of activity, in the form of neurolytic mixtures, in addition to other measures such as blood, heterogenic protein and synthetic blood substitutes. The use of neurolytic mixtures is based on the fact that, while they act mainly on the central nervous system, they at the same time effect a pharmacological block of the autonomic nervous system, and this prevents the excessive liberation in shock of adrenalin, acetylcholine, histamine and histamine-like substances, thereby decreasing the severity of the reaction of the body [14]. Furthermore, certain drugs included in the lytic mixture affect the carbohydrate metabolism [9]. As investigations have shown [6, 10, 11, 12], in traumatic shock considerable changes are observed in the biochemical blood indices (a fall in the alkali reserve, a lowering of cholinesterase activity and a rise in the blood sugar).

In view of the fact that, after administration of heterogenic protein blood substitutes, complications of an anaphylactic character could arise, we made a comparative study of the effect of a neurolytic mixture on certain biochemical blood indices during the prophylaxis of anaphylactic shock and during the treatment of traumatic shock complicated by anaphylactic shock.

EXPERIMENTAL METHOD

For this purpose we carried out three series of experiments on 30 rabbits. In the first, control, series we studied the biochemical changes in the blood in anaphylactic shock without the use of a neurolytic mixture. In the second series the biochemical changes in the blood were studied with the use of a neurolytic mixture for the prevention of anaphylactic shock. In the third series the biochemical changes in the blood of rabbits were studied during the treatment of traumatic shock, complicated by anaphylactic shock, with a neurolytic mixture.

In the first series of experiments sensitization was induced by giving two subcutaneous injections of 1 ml of ox serum at intervals of 7-10 days. From 10 to 15 days after the second injection of antigen, the experimental animals were used in the main experiment. Anaphylactic shock was caused by the intravenous injection of an assaulting dose (3 ml) of ox serum. The changes in the arterial pressure and in respiration were recorded on the smoked frum of a kymograph by the usual method. Before the experiment and after the intravenous injection of the assaulting dose of antigen determinations were made of the sugar level in whole blood by the Hagedorn-Jensen method, the alkali reserve of the plasma by Van Slyke's method, and the cholinesterase activity by the methods of Zubkova and Pravdich - Neminskaya. Blood for these tests was taken, in a volume of 5 ml, from the carotid artery.

In order to prevent anaphylactic shock we used the following neurolytic mixture: chlorpromazine (2%, 0.5 ml), pentamine (2%, 0.5 ml), benadryl (2%, 0.5 ml) and promedol (2%, 0.5 ml). Before the intravenous injection of the neurolytic mixture the initial levels of the blood sugar, the alkali reserve and the cholinesterase activity were determined. These were subsequently determined 10 minutes, and in some experiments 20 minutes,

TABLE 1

Changes in the Levels of the Blood Sugar, Alkali Reserve and Cholinesterase Activity in Anaphylactic Shock

Type of test	Experiment No.	Initial values	After inject. of antigen	Difference from initial values	Difference (in %)	During shock	Difference from initial values	Difference (in %)	Result
Blood sugar, in mg %	1	120	149	+29	+24	Died			
	2	88	142	+54	+61	172	+84	+95	Died
	3	92	135	+43	+46	171	+79	+85	Died
	5	121	136	+15	+12	Died			
	14	165	246	+81	+49	Died			
Mean		117	161	+44	+37	171	+81	+90	
Alkali reserve of the plasma, in volumes %	1	41,4	30,9	—10,5	—25	Died			
	2	37,3	28,3	—9,0	—24	22	—15,3	—41	Died
	3	41,2	35,4	—5,8	—14	24,9	—16,3	—39	Died
	5	34,2	34,2	0	0	Died			
	14	21,4	15,7	—5,7	—27	Died			
Mean		35,1	28,9	—6,2	—17	23,4	—15,8	—40	
Cholinesterase activity of the plasma, in cm^3 of 0.01 N NaOH solution	1	0,31	0,17	—0,14	—45	Died			
	2	0,38	0,19	—0,19	—50	No determination possible			
	3	0,26	0,18	—0,08	—33	0,14	—0,12	—53%	Died
	5	0,36	0,2	—0,16	—44	Died			
	14	0,18	0,08	—0,1	—55	Died			
Mean		0,3	0,16	—0,14	—46				

after the intravenous injection of the neurolytic mixture, and again 5-10 minutes, and in some experiments 30 minutes, after the intravenous injection of the assaulting dose of antigen. In the third series traumatic shock was induced by repeated stimulation of the sciatic nerve with the electric current from an induction coil, the distance between the primary and secondary coils of which was 5-6 cm. The stimulation lasted 2 minutes and the interval between stimulation was 2-5 minutes. After stimulation of the sciatic nerve, the animal was bled to the extent of 1 % of the body weight (15-20 ml). The neurolytic mixture was injected intramuscularly and intravenously 15 minutes after the end of stimulation of the sciatic nerve, when the arterial pressure had fallen persistently by 40-50% of its initial level and showed no tendency to rise, and also other features of traumatic shock were observed. From 10 to 15 minutes after injection of the neurolytic mixture the assaulting injection of antigen was given. In 5 experiments, before giving the mixture, physiological saline and 5% glucose solution were injected intravenously in a volume of 15-20 ml. Blood for biochemical investigation was taken from the carotid artery before the experiment, after the end of stimulation of the sciatic nerve, after injection of the neurolytic mixture and after intravenous injection of the assaulting dose of ox serum.

EXPERIMENTAL RESULTS

Intravenous injection of the assaulting dose of antigen was accompanied by the development of anaphylactic shock with a lethal outcome. The arterial pressure at the moment of injection of the serum and immediately after the end of the injection was raised, the respiration rate was quickened considerably, and the general behavior of the experimental animal was quiet. From 1 to 2 minutes after the end of the injection of antigen the arterial pressure rapidly (in the course of 3-5 minutes) fell to zero, respiration became slower and more superficial and finally ceased, contractions of the heart being observed for a further 3-5 minutes.

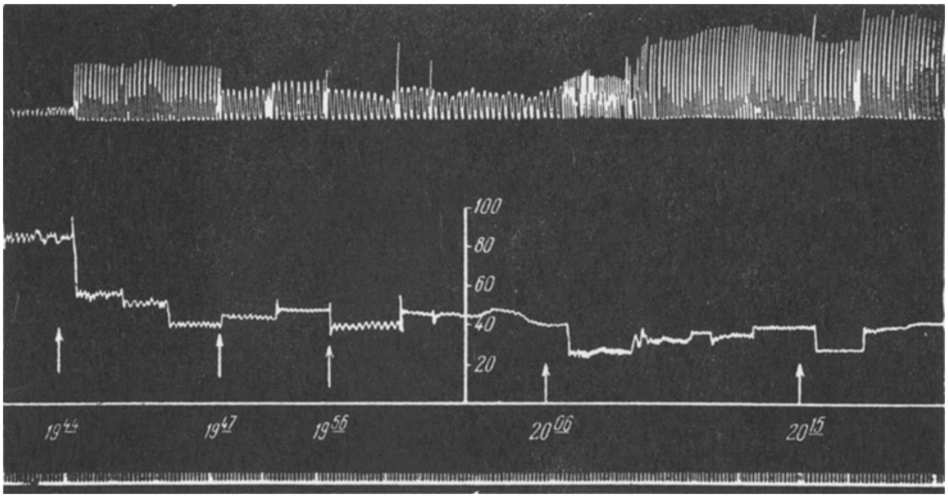

Fig. 1. Changes in the arterial pressure and respiration during prophylaxis of anaphylactic shock by the intravenous injection of a neurolytic mixture. 19 hours 44 minutes: blood taken for biochemical tests and injection of neurolytic mixture. 19 hours 56 minutes: blood taken for biochemical tests. 20 hours 06 minutes: intravenous injection of assaulting dose of ox serum. 20 hours 15 minutes: blood taken for biochemical tests. 20 hours 30 minutes: blood taken for biochemical test and end of experiment. Significance of the curves (from above down): respiration, arterial pressure, zero line, time marker.

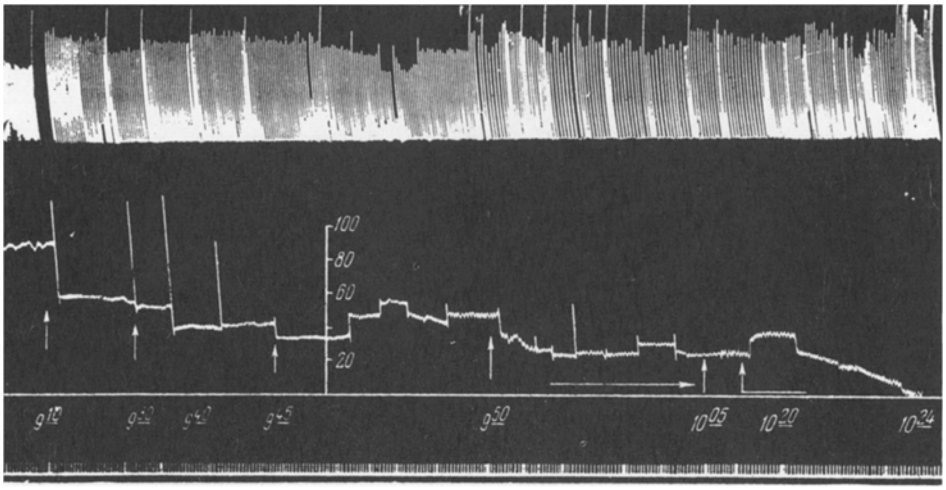

Fig. 2. Change in the arterial pressure and respiration in anaphylactic shock developing on a background of traumatic shock. 9 hours 10 minutes: bleeding (↑), 9 hours 30 minutes – 9 hours 40 minutes: stimulation of the sciatic nerve (↑), 9 hours 45 minutes: blood taken for biochemical tests (↑), 9 hours 45 minutes – 9 hours 49 minutes: intravenous injection of physiological saline (30 ml), 9 hours 50 minutes – 10 hours 05 minutes: intravenous injection of neurolytic mixture (→), 10 hours 20 minutes: intravenous injection of assaulting dose of antigen (5 ml), 10 hours 24 minutes: death of rabbit. Significance of the curves (from above down): respiration, arterial pressure, zero line, time marker.

It will be seen from the findings in Table 1 that, in anaphylactic shock, the alkali reserve fell by between 17–40% and the cholinesterase by an average of 46%, while the blood sugar rose by 37–90% of its initial level. These changes were the greater the more severe the course of the anaphylactic shock. The indices showing the

TABLE 2

Changes in the Levels of the Blood Sugar, Alkali Reserve and Cholinesterase Activity after Injection of a Neurolytic Mixture

Type of test	Experiment No.	Initial values	After inject. of mixture after 10 min	After inject. of mixture after 20 min	Difference from initial values, in %	After inject. of antigen after 10 min	After inject. of antigen after 30 min	Difference from initial values, in %	
Blood sugar (in mg%)	6	172	231	—	+34	237	—	+37	Lived
	7	94	114	—	+21	140	—	+48	Lived
	13	87	118	—	+35	112	112	+28	Lived
	15	96	568	—	+491	Died			
	16	138	155	129	+1	150	—	+17	Lived
	17	128	140	129	+1	150	—	+17	Lived
	18	398	407	—	+2	Died			
	21	101	149	152	+50	190	—	+86	Lived
	22	135	146	128	—5	193	198	+46	Lived
Mean . . .		108	186	167	+43	184	142	+67	
Alkali reserve, in volumes %	6	42,4	42,4	—	0	Could not be determined			
	7	38,5	53,8	—	+39	51	—	+32,4	Lived
	13	39,5	42,4	—	+7,3	43,3	38,5	—2,5	Lived
	15	24,2	22,3	—	—7,8	Died			
	16	52,8	51,9	—	—1,7	43,3	—	—17	Lived
	17	41,4	48,1	48,1	+16	27,1	—	—36,4	Lived
	18	29	29	—	0	Died			
	21	46,2	42,4	49	+6	39,5	—	—14,4	Lived
	22	—	37,5	—	—	26		—30,6	Lived
	23	36,6	42,4	44,3	+21	40,4	30	—18	Lived
Mean		42,5	45,1	47,1	+14	38,6	34,2	—10	
Cholinesterase activity, in cm^3 of 0.01 N NaOH solution	6	0,18	0,24	—	+30	0,21	—	+5	Lived
	7	0,23	0,27	—	+17,3	0,13	—	—43,4	Lived
	13	0,27	0,26	—	—4,4	0,15	0,14	—48	Lived
	15	0,13	0,08	—	—37	Died			
	16	0,27	0,27	—	0	Could not be determied			
	17	0,19	0,19	0,19	0	0,18	—	—5	Lived
	18	0,24	0,2	—	—16,6	Died			
	21	0,36	0,33	0,19	—46	0,19	—	—46	Lived
	22	0,25	0,21	0,22	—12	0,17	0,17	—32	Lived
	23	0,23	0,22	0,2	—13	0,2	0,2	—13	Lived
Mean		0,25	0,25	0,2	—17	0,18	0,17	—31	

greatest changes in the blood in shock were those of the cholinesterase activity, for they were recorded at times when the other indices were unchanged or were changed only insignificantly (rabbit No. 5).

Intravenous injection of a neurolytic mixture for prophylaxis of anaphylactic shock led to a fall in the arterial pressure by 50-60% of its initial value, and the more rapidly the mixture was injected, the greater the fall in the pressure. Two of the rabbits died during rapid injection. Immediately after injection of the mixture the respiration rate increased, and 2-3 minutes later it became slow (10-12 respirations per minute) and superficial, with a decrease in the amplitude of the respiratory movements.

TABLE 3

Changes in the Levels of the Blood Sugar, Alkali Reserve and Cholinesterase Activity during Traumatic Shock

Type of test	Experiment No.	Initial level	Traumatic shock	Difference, in %	Injection of mixture	Difference from initial value, in %	Injection of antigen	Difference from initial value, in %	Result
Blood sugar, in mg %	8	86	140	+62	147	70	154	+78	Died
	9	96	186	+93	294	206	306	+216	Died
	10	193	281	+45	376	94	Died		
	11	117	215	+83	185	+58	181	+54	Died
Mean. . . .		123	205	+66	250	+103	214	+65	
Alkali reserve, in volumes %	8	35,7	12,8	—65	9,9	—72	6,6	—78	Died
	9	24	14	—41	14	—41	Could not be determined		
	10	26,2	9,9	—63	12,8	—54	Died		
	11	30	6,9	—77	14,7	—51	15,7	—41	Died
Mean . . .		29	10,9	—62	12,8	—55	11,1	—59	
Cholinesterase activity of the plasma in cm^3 of 0.01 M NaOH solution	8	0,51	0,36	—29	0,35	—31	0,18	—65	Died
	9	0,35	0,33	—5,7	0,26	—26	0	—100	Died
	10	0,35	0,35	0.	0,12	—65	Died		
	11	0,25	0.24	—4	0,12	—52	0,03	—88	Died
Mean		0,36	0,31	—13	0,21	—14	0,1	—84	

The intravenous injection of the assaulting dose of ox serum was accompanied by a doubling of the respiration rate in the course of 10-12 minutes, and subsequently it remained rather high until the end of the experiment, being higher than after the injection of the neurolytic mixture but lower than before the drugs were given.

After a brief rise, the arterial pressure fell in response to the injection of the assaulting dose of antigen rather below the level which was found 10 minutes after injection of the mixture and at the end of the experiment it rose slowly to 60-70 mm (Fig. 1).

All the experimental animals of this series tolerated satisfactorily the intravenous injection of the assaulting dose of ox serum, and on the following days their behavior was indistinguishable from normal.

In Table 2 are shown the changes in certain biochemical blood indices which took place after injection of a neurolytic mixture for prophylaxis of anaphylactic shock.

In this series of experiments the blood changes determined by means of the biochemical tests arose both under the influence of the neurolytic mixture and of the antigen. In rabbit No. 15, the blood sugar rose by almost 500% in the course of 2-3 minutes, the cholinesterase activity fell by 37% and the alkali reserve was almost unchanged. In rabbit No. 18 the variations in these indices were minimal.

After 10 minutes, the slow intravenous injection of the neurolytic mixture caused an increase in the blood sugar of 72% on the average, but after 20 minutes the level fell, although it still exceeded the initial level by 43% on the average.

The assaulting dose of ox serum caused a moderate increase in the blood sugar by comparison with the level found in the previous determinations, although the mean figures were unchanged. The alkali reserve of the plasma increased in all the experiments under the influence of the neurolytic mixture by an average of 6.1%

after 10 ,minutes and by 14% 20 minutes after injection of the mixture. Injection of the antigen lowered this level in some cases only when compared with the maximal figures established after injection of the preparations, and it stayed above the original values, falling by an average of 9.1-10.1% of the initial value.

After injection of the mixture the variation in the cholinesterase activity took the form of either an insignificant increase or decrease. Twenty minutes after injection the cholinesterase activity fell very moderately in relation to the previous determination and by 25.5-31.0 % in relation to its initial value.

Traumatic shock, as already pointed out, was caused by stimulation of the sciatic nerve with an electric current after preliminary bleeding. The bleeding itself led to a fall in the arterial pressure, on the average by 18 mm. Under these circumstances, in some experiments the respiration rate increased by 4-10 per minute, while in others it remained slower.

After bleeding, traumatic shock developed after 5-10 stimulations of the sciatic nerve. The arterial pressure fell by 30-40 mm from the level established after bleeding, the corneal reflex became sluggish and respiration became embarrassed, and moreover, in some experiments it was rapid, whereas in others, after a period of increased rate, respiration became slow and embarrassed, especially the phase of inspiration. When the picture of traumatic shock was fully developed, the intravenous injection of the neurolytic mixture led to a catastrophic fall in the arterial pressure (in 5 rabbits to zero) and to death of the animals within the next 5 minutes. In 6 experiments the pressure after injection of the mixture settled at between 18 and 25 mm Hg. In one case death from traumatic shock took place even before injection of the mixture.

The subsequent (10-15 minutes after injection of the mixture) intravenous injection of the assaulting dose of antigen led to a rapid fall in the arterial pressure to zero and to death of the experimental animals within 3-5 minutes. The intravenous infusion of 5% glucose solution and physiological saline, in volumes of 20-30 ml, both before injection of the neurolytic mixture in the course of development of traumatic shock and together with the mixture after stimulation of the sciatic nerve, did not prevent death of the animals from the intravenous injection of the assaulting dose of ox serum (Fig. 2).

The results relating to the changes in the blood sugar, alkali reserve and cholinesterase activity are shown in Table 3 .

As may be seen from the figures in Table 3, the onset of traumatic shock was characterized by a rise in the blood sugar and a fall in the alkali reserve. The cholinesterase activity fell moderately, on the average by 13%.

Under the influence of the intravenous injection of the neurolytic mixture the blood sugar rose and the variations in the alkali reserve took the form of both a decrease and an increase. This feature must evidently be interpreted not as a true increase in the alkali reserves of the blood, but as the result of an increase in the carbon dioxide, due to the slowing of the respiration after injection of the neurolytic mixture, which essentially lowered the ventilation volume of the lungs and the sensitivity of the respiratory center. It must also be remembered that there was a possibility of gaseous acidosis on account of stasis of the blood in the capillaries in association with the lowered velocity of the blood flow.

The injection of the neurolytic mixture into rabbits in a state of traumatic shock caused, in contrast to control experiments, a marked fall of 41% in the cholinesterase activity.

After injection of the assaulting dose of antigen all the rabbits died from anaphylatic shock. In relation to the blood sugar a tendency for this to fall was observed, from 250 to 214 mg%, which could evidently be accounted for by exhaustion of the glycogen reserves of the liver. The value of the alkali reserve before death of the experimental animal fell by 41% by comparison with the initial values, and rose slightly in relation to the minimum level observed during the experiment (on the average from 6.9 to 15.7 volumes %).

SUMMARY

The biochemical changes occurring in the blood (blood sugar level, alkali reserve, cholinesterase activity) were insignificant when the neurolytic mixture (2% solutions of chlorpromazine , pentamine, promedol and benadryl) was employed for preventing anaphylactic shock .

The administration of this mixture in the instance of a fully developed traumatic shock not only does not prevent the development of anaphylactic shock, but even aggravates both the course and the outcome of the

traumatic shock. This is confirmed by the biochemical changes in the blood: in comparison with the changes observed in experiments on the prophylaxis of anaphylactic shock with the neurolytic mixture, blood sugar rose 2.4 times, the alkali reserve dropped 5 - 5.9 times and cholinesterase activity fell 2.4 - 2.7 times.

LITERATURE CITED

[1] A. D. Ado and M. A. Erzin, Collected Works of the Kazan' Medical Institute. Works of the Theoretical Departments, Collections 9-10 (3-4), 241-251 (Kazan', 1933) [In Russian].

[2] B. S. Bamdas, G. D. Glad and L. I. Lando, Zhur. Nevropatol. i Psikhiat. 2, 121-138 (1956).

[3] F. R. Vinograd-Finkel', Problemy Gematol. i Pereliv. Krovi, No. 5, 49-54 (1956).

[4] V. I. Volkotrub, Author's abstract of candidate's dissertation (Leningrad, 1949). [In Russian].

[5] P. T. Gorbunov, Proceedings of a Scientific Meeting to Commemorate the 35th Anniversary of the Minsk Medical Institute, 64-65 (Minsk, 1956). [In Russian].

[6] A. N. Gordienko and T. A. Nazarova, Byull. Éksptl. Biol. i Med. 19, 4-5, 34-36 (1945).

[7] V. S. Kiselev, Proceedings of the Jubilee Scientific Meeting to Commemorate the Bicentenary of the Moscow Medical Institute, Theoretical Section 23 (Moscow, 1955). [In Russian].

[8] N. G. Krol', Collected Works of the Kazan' Medical Institute. Works of the Theoretical Departments, Collection 9-10 (3-4), 238-240 (Kazan', 1933). [In Russian].

[9] M. D. Mashkovskii, Zhur. Nevropat. i Psikhiat. 2, 81-93 (1956).

[10] T. E. Petkun, Klin. Med. 6, 39-43 (1945).

[11] I. R. Petrov, Klin. Med. 4, 3-11 (1947).

[12] V. I. Popov, Shock, 81-87 (Kiev, 1938). [In Russian].