SPECIFIC FEATURES OF THE ANIMAL REACTION TO A SHOCK-INDUCING STIMULUS FOLLOWING THE ADMINISTRATION OF AMINAZINE*

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Neuroplegic substances of the phenothiazine series, especially Aminazine, have recently begun to be used to prevent and treat traumatic shock.

Laborit and Huguenard [5, 6] were the first to point out the value of Aminazine in traumatic and surgical shock. They believe, as do several other authors [1, 3], Aminazine's positive effect in shock to be due to its intensification of the processes of intrinsic inhibition and of inhibition in the zone of the reticular formation in particular.

Under experimental conditions, G. D. Chesnokova and B. A. Agaev [4] observed Aminazine to exert a favorable effect on animals in traumatic shock and then corroborated these data with clinical observations.

The purpose of this investigation was to further analyze Aminazine's effect on the course of traumatic shock. Since traumatic shock is a phasic process, we decided first to determine Aminazine's effect on the course and issue of shock changes depending on the phase in which the substance is administered.

Then, because Aminazine's hypotensive effect could be harmful in shock, we also determined the efficiency of its use in conjunction with vasopressor substances.

EXPERIMENTAL METHOD

The experiments were performed on nonanesthetized cats. Shock was induced by A. M. Dubinskii's method; the right paw of the animal was stimulated with a pulsating current four pulses per sec in frequency, 100 ma current force at the the height of each pulse and a stimulus duration of 0.08 msec. A kymograph was used to record the respiration and arterial pressure (in the femoral artery) throughout the experiment, the rectal temperature was taken and the general condition of the animal observed.

EXPERIMENTAL RESULTS

Thirty-five control experiments were performed in order to determine the characteristic course of the shock induced by the above method. These observations allowed us to distinguish three separate phases in the development of the shock: the erectile phase, torpid phase I and torpid phase II.

During the erectile phase of shock, we observed acute excitation of the animal, retarded respiration, a rise of arterial pressure to 180-200 mm of mercury and acceleration of the pulse. Torpid phase I was characterized by apathy, rapid, shallow respiration, the fall of arterial pressure and a decreased number of cardiac

* Chlorpromazine – Publisher.

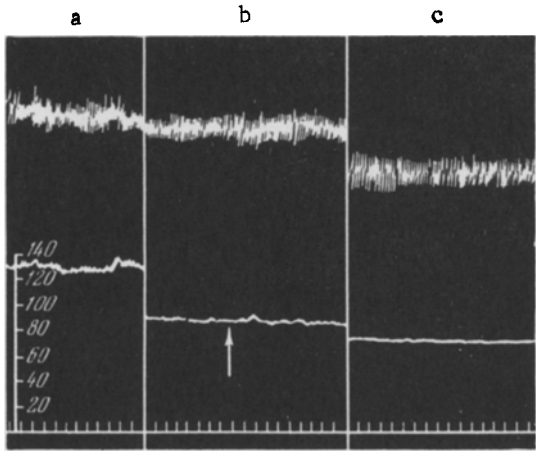

Fig. 1. Change in respiration and arterial pressure following administration of Aminazine during torpid phase I. 1) Original condition; b) during Aminazine administration (torpid phase I); c) one hour and 15 min after Aminazine administration. Curves show (from top to bottom): respiration; arterial pressure; time in 3-second marks. Arrow (↑) shows Aminazine administration.

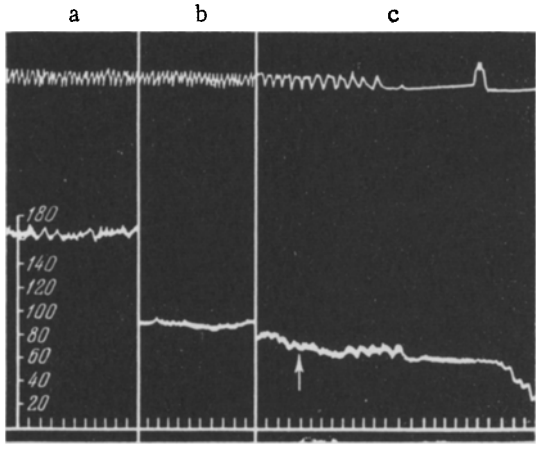

Fig. 2. Change in respiration and arterial pressure following Aminazine administration during torpid phase II. a) Original condition; b) torpid phase II; c) shock during Aminazine administration. Symbols the same as in Fig. 1.

contractions. Further retardation of the respiration, a steady fall of arterial pressure to 40-50 mm of mercury and retardation of the pulse were usually observed during torpid phase II.

We then studied the effect of Aminazine administered during the various phases on the course and issue of the shock. Aminazine was intramuscularly injected in a dose of 5 mg/kg on a background of the maximal arterial pressure. In the erectile phase of shock (7 experiments), a gradual fall of arterial pressure to 70-80 mm of mercury usually began 2-3 min after the Aminazine injection and then remained stable at the new level for a long time, despite continuing stimulation. There was not much change in the heart rate or that of the respiration. In these experiments, the more advanced phases of shock could only be induced by prolonged stimulation lasting 1-1½ hours, while only 30-40 min of stimulation were required to produce an analogous condition in the control experiments. Another difference from the control was that cessation of stimulation was followed by a stable rise of arterial pressure to 80-90 mm of mercury, even in cases when torpid phase II of shock was clinically apparent. The administration of Aminazine during the erectile phase rapidly diminished the animal's excitation and greatly reduced its response to extrinsic stimuli (touches, pricks).

The effect of Aminazine on the course of shock in torpid phase I was examined in 13 experiments.

In all the experiments, torpid phase I of shock was observed to be protracted and slow to change into torpid phase II. For example, torpid phase I of shock lasted an average of 25-30 min in the control experiments, but in the experiments with Aminazine, its duration stretched to 40-45 min, and more in some cases. After the administration of Aminazine, the arterial pressure decreased from the level usually characterizing torpid phase (90-100 mm of mercury) to 65-75 mm of mercury and then remained constant at the latter level. Slight acceleration of the respiration and pulse was observed (Fig. 1). The animals remained sluggish and apathetic both during the experiments and for quite a long while afterwards.

Torpid phase II of the shock was successfully developed in all 13 experiments by prolonging the action of the pulsating current on the animals; the arterial pressure, however, rose from 60 to 80-95 mm of mercury after stimulation ceased, which did not occur in the control animals.

The survival rate of the animals was also higher in the experiments; six out of the 13 cats given Aminazine during torpid phase I of shock and in which torpid phase II had clinically developed survived, while only one out of 15 animals survived in the analogous control experiments.

In five experiments, Aminazine was administered during torpid phase II of shock. In every case, the preparation was injected on a background of rather low arterial pressure (about 50 mm of mercury) and retarded pulse and respiration. After the Aminazine injection, further retardation of the respiration and heart rate was

usually observed along with a rapid fall of arterial pressure. The latter fell from 50-40 to 20-10, often even to 0 mm of mercury within 2-5 min, and the animal died (Fig. 2).

Aminazine, therefore, alters the course of shock and makes animals more resistant to a shock-inducing stimulus when administered during the erectile phase or torpid phase I of shock. However, Aminazine is known to possess a pronounced hypotensive effect, which considerably limits its use in shock. To prevent the development of hypotonia after the administration of Aminazine, B. I. Lyubimov [2] recommends that it be administered in conjunction with either Pituitrin or noradrenalin.

In a previous work, we established that both noradrenalin and Pituitrin, when administered under conditions of experimental shock, induce a rise of arterial pressure and its stabilization at the new level; Pituitrin has the more lasting effect of the two. On this basis, we used Pituitrin in this work to prevent Aminazine-induced hypotonia.

In the experiments conducted to determine the effect of the Aminazine-Pituitrin combination on the course of shock, Aminazine was intramuscularly injected in a dose of 5 mg/kg, as in the previous experiments, and then, as soon as the arterial pressure showed a tendency to fall, 1 ml Pituitrin containing 3 units was administered.

In five experiments, Aminazine and Pituitrin were administered in torpid phase I of shock. In every case, the arterial pressure rose 20-30 mm of mercury a few minutes after the administration of Pituitrin and was restored to the initial level within 10-15 minutes despite continuous application of the stimulation. It was interesting that the respiration and heart rate hardly changed at all during these experiments. All five animals of this group survived despite prolonged application of the stimulation and the fact that the shock reached a depth corresponding to torpid phase II.

In the next five experiments, Aminazine and Pituitrin were administered during torpid phase II of shock, and the acute fall of arterial pressure observed when Aminazine was administered alone during this phase of shock did not occur in any of these experiments.

In three experiments of this series, the administration of Pituitrin increased the severity of the shock, and the animals died 40-50 min afterwards; one animal died later than this, but within the first 24 hours after the experiment, and one animal survived.

The data presented demonstrate that Aminazine used in conjunction with Pituitrin during torpid phase I and even torpid phase II of experimental shock has a positive effect on the course and issue of the shock. G. D. Chesnokova and B. A. Agaev [4] observed, as we did, Aminazine to exert a favorable therapeutic effect when administered at early stages of shock; when it was administered during stage III (analogous to our torpid phase II), however, the death of the animals was expedited. In order to ensure the maintenance of a sufficiently high arterial pressure level, they proposed the use of blood transfusion before the administration of Aminazine. It is hardly expedient to increase the total blood volume, however, in shock cases,where there is no blood loss and there is a decrease in the volume of the circulating blood due to the development of capillary stasis. In such cases, we believe it more effective to limit dystonia of the peripheral vessels by the use of vasopressor substances with a prolonged effect, such as Pituitrin, for example, which we used in our experiments.

SUMMARY

The author studied peculiarities attending the course of experimental shock with Aminazine (largactyl) administered during its various phases (erectile, the I and the II torpid). Aminazine therapy proved to be the most effective during the erectile and the I torpid phases, whereas its use during the II torpid phase leads to rapid death of the animals.

The hypotensive properties of Aminazine limit the possibilities of its application in shock. Therefore, it is best to administer it in conjunction with vasopressor substances. Combined Aminazine – Pituitrin administration provokes a positive therapeutic effect on the course and the outcome of an experimental shock.

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