USE OF THE ARTIFICIAL CIRCULATION FOR RESUSCITATING ANIMALS AFTER PROLONGED CLINICAL DEATH IN DEEP HYPOTHERMIC CONDITIONS

V. I. Soboleva, S. A. Mushegyan, and N. A. Super

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Deep hypothermia is a very promising method of ensuring survival in severe hypoxia and of prolonging the period of clinical death. The method most widely used at the present time is that of extracorporeal cooling of the blood by means of an artificial circulation apparatus equipped with a special thermoregulatory device. Several authors [10] who have used this method have succeeded in lowering the body temperature of dogs to 1-3°, and of restoring the animals to life after exclusion of the heart for 45-50 min.

Previous experiments undertaken in the laboratory [5] have shown that by means of a fairly simple method—intra-arterial infusion of blood accompanied by withdrawal of blood from a vein, artificial respiration, electrical defibrillation, and electrical stimulation of the heart—the vital functions of several dogs could be restored after clinical death caused by acute exsanguination in deep hypothermic conditions lasting for 2 h. However, in these experiments a number of complications developed either in the cooling process or in the recovery period, which interfered with the process of restoration of the vital functions, so that only a few animals survived (10 of 31).

Histological investigation [6] of these animals revealed severe changes in the brain and internal organs. However, with an increase in the period of survival after resuscitation, signs of repair processes became clearly defined.

To overcome the factors complicating the process of cooling and resuscitation, the experiments of the present series were carried out, in which an artificial circulation created by means of an apparatus with a thermoregulatory device, was used for cooling, resuscitation, and subsequent reheating.

EXPERIMENTAL METHOD

Experiments were carried out on 20 dogs. Before the experiment the animals received a subcutaneous injection of 2% Pantopon solution (0.1 mg/kg). Heparin was used to stabilize the blood. Before cooling began and at intervals during cooling, 0.2% Nembutal solution was injected by the intravenous drip method. An artificial circulation using the AIK-RP-64 apparatus, fitted with a heat-exchanger, was used for cooling, resuscitation, and subsequent reheating.

When the body temperature had fallen to 8-10° the perfusion was stopped, and the time of clinical death was counted from the moment of ending the withdrawal of blood from the animal. After clinical death had lasted 2 h, resuscitation was started by application of the artificial circulation in conjunction with artificial respiration, and if fibrillation developed, electrical defibrillation was carried out. After recovery of the cardiac activity, the system of operation of the apparatus was changed in accordance with the hemodynamic indices. The artificial circulation was stopped when the animal's body temperature reached 33-35° (40-60 min from the beginning of resuscitation). The arterial and venous pressure, the electrocardiogram (EGG), and in some animals the electroencephalogram (EEG) were recorded during the experiment.

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EXPERIMENTAL RESULTS

The cooling period lasted for between 26 min and 1 h 20 min. When the body temperature had fallen to 26-16°, the dogs developed ventricular fibrillation, often followed by asystole in the later stages of cooling. In most of the animals the fibrillation was stopped during cooling (sometimes repeatedly) by means of condenser discharges (2500-4000 V). When the body temperature was 8-10°, infrequent biphasic wave-complexes or (in the presence of fibrillation) polymorphic low and arrhythmic waves were recorded on the ECG. When perfusion stopped the bioelectrical activity of the heart was extinguished for a few minutes [8].

During fibrillation and asystole the artificial perfusion was continued to lower the temperature still further. During this period the arterial pressure was maintained at the level of 30-70 mm. In the low temperature conditions this level was apparently adequate for maintaining the vital activity of the brain, for the EEG showed that the bioelectrical activity of the brain stopped altogether when the body temperature was 8-10°.

The fact that in these animals the electrical activity of the brain persisted for such a long time may probably be attributable to the use of artificial perfusion, for according to reports in the literature [1, 4, 7, 9], in experiments with hypothermia when no artificial circulation was used, this activity ceased at higher temperatures (from 15-20°).

During cooling, respiration ceased in most animals early (at the 5th-7th min of cooling), at an even higher body temperature (26.5-28°). In a few dogs it ceased at the 12th-13th min of cooling, at a temperature of 12-16°. Soon after respiration stopped, the corneal reflexes disappeared.

Throughout the period of cooling, despite the early cessation of respiration, no arterial hypoxemia was present. The oxygen saturation of the arterial blood was near the 100% level. The total concentration of organic acids remained within the initial limits (9.2-12 meq/liter).

After clinical death lasting 2 h, in the initial period of resuscitation, all the animals developed ventricular fibrillation. With an increase in the body temperature the amplitude of the fibrillations rose sharply (from 0.1-0.2-1.2-2.5 mV), and the ECG began to show predominantly a regular rhythm with a frequency of 500-600 per min. After the appearance of rapid fibrillation of the ECG, defibrillation was started. The cardiac activity was restored in 17 dogs 10-23 min after the beginning of resuscitation when the body temperature was 14-22°. In one animal it appeared later—at the 37th min of resuscitation. In two dogs, because of acute dilatation of the heart caused by inadequate perfusion, the cardiac activity could not be restored.

The appearance of the ventricular complexes after defibrillation at a body temperature close to 20° was considerably modified, but the degree of widening and deformation of the QRS complex was less marked than at the same temperatures during cooling. This was evidently due to the higher temperature of the heart than that measured in the rectum, because the warm blood used for perfusion quickly entered the coronary vessels. Ther normal ECG complexes were restored when the body temperature was 31-35°. The rapid return to the normal ECG demonstrated the reversible character of these changes.

Respiration reappeared 1-10 min after the resumption of cardiac activity, and in some dogs even 1-5 min before this took place. The corneal reflexes of the 12 resuscitated dogs returned at the 11th-33rd min of resuscitation when the body temperature was 18.5-30.5°, and in the other dogs rather later—from 44 min to 2 h 46 min, when the body temperature was 31-35°. The first signs of recovery of the electrical activity of the brain recorded in three dogs appeared 8-10 min after restoration of the corneal reflexes (these were restored in these animals 27, 34, and 44 min after the beginning of resuscitation).

Continous electrical activity was restored by the end of the second hour of resuscitation. On emerging from the state of hypothermia, the dogs showed moderate metabolic acidosis. For example, the maximal concentration of organic acid in the blood, although elevated to 14-20 meq/liter, was nevertheless increased much less than in analogous experiments without the use of the artificial circulation [2]. The level of organic acid was within normal limits 5-8 h after the beginning of resuscitation. Of the 18 animals undergoing resuscitation, 9 recovered completely. Most dogs regained sight and hearing at the end of the first or second day and one began to see on the 5th day. On the 3rd or 4th day, 4 animals were outwardly almost indistinguishable from healthy dogs, while in 5 dogs (in 3 of which conditioned reflexes had been formed) coordination of movement was disturbed for a considerable time (21-35 days), after which it recovered. The remaining 9 dogs undergoing resuscitation died between 1 and 6 days after its beginning: one animal

died from pneumonia, the body temperature of another could not be lowered below 18° during clinical death, a 3rd died from hyperthermia developing in the recovery period; 6 dogs developed cardiovascular failure. At necropsy on these animals extensive hemorrhages were found in the heart muscle. The reason was evidently inadequate perfusion, both during cooling and in the recovery period.

A study of the conditioned-reflex activity of three dogs resuscitated from clinical death showed that the disturbances of the functions of the higher levels of the brain developing in these circumstances were reversible in character. A dynamic stereotype consisting of positive and inhibitory conditioned reflexes (developed in response to stimuli addressed to the auditory and optic analyzers) was restored 3-4 weeks after resuscitation.

The brain can be made to tolerate a longer period of clinical death in conditions of deep hypothermia than in those of moderately deep hypothermia, according to the observations of M. S. Gaevskaya and E. A. Nosova [3], by the accumulation of an excess of carbohydrates in the cerebral cortex during cooling to temperatures below 25° and by the longer preservation in the brain tissues of high-energy phosphorus compounds during the period of dying and of clinical death.

The comparatively rapid recovery of cardiac activity and respiration, the absence of metabolic acidosis during cooling and the presence of moderate acidosis in the recovery period, the early appearance of the first signs of bioelectrical activity of the brain during resuscitation, and also the complete recovery of the function of the higher levels of the brain all indicate the advantages of the use of the artificial circulation apparatus for these purposes, and also emphasize the potential opportunities for resuscitation presented by animals withstanding clinical death for 2 h in the conditions of deep hypothermia.

LITERATURE CITED

1. N. V. Bratus', Pat. Fiziol., No. 2, 23 (1958).
2. O. N. Bulanova, Pat. Fiziol., No. 2, 26 (1965).
3. M. S. Gaevskaya and E. A. Nosova, in the book: Collected Proceedings of the 3rd All-Union Conference on Biochemistry of the Nervous System [in Russian], 421, Erevan (1963).
4. L. I. Murskii (Editor), Hypothermia of the Brain [in Russian], Vladimir (1965).
5. V. A. Negovskii, V. I. Soboleva, et al., Byull. éksp. Biol., No. 11, 39 (1963).
6. N. P. Romanova, Arkh. Pat., No. 6, 69 (1966).
7. P. M. Starkov (Editor), The Problem of Acute Hypothermia [in Russian], 15, Moscow (1957).
8. V. Ya. Tabak and V. I. Soboleva, in the book: Current Problems in Preanimation and Hypothermia [in Russian], 75, Moscow (1964).
9. T. Gänschirt, et al., Arch, exp. Path. Pharmak., 222, 431 (1954).
10. F. Gollan, R. Phillips, et al., J. thorac. Surg., 30, 626 (1955).