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Deep hypothermia as a means of prolonging clinical death

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The first steps in the study of deep hypothermia in mammals were taken in investigations on small animals (marmots, hamsters and rats). Their results demonstrated convincingly that the body temperature of these animals could be lowered artificially to 0-5°C, and even below zero (°C), for a period of 1-2 hr, after which all the vital functions could be restored simply by reheating (5, 7, 8, 14 and 15). Reports first published in 1952 (10) showed that the heart could be excluded from the circulation during deep hypothermia in higher, warm-blooded animals. Various authors (11 and 12) managed to lower the body temperature of dogs to 1-3°C by the use of an extracorporeal circulation incorporating a perfusion apparatus and a special device for controlling the temperature, and after excluding the heart for 45-60 min, they were able to revive the animals. Many experimental and clinical observations on this subject have been described (1, 3, 4, 6, 9, 13 and 18).

The object of the present investigation was to try to restore the vital functions of dogs after long periods of clinical death from acute blood loss under deep hypothermia and to assess the factors hindering and assisting recovery.

METHODS

Experiments were conducted on 31 dogs. Before the experiments the dogs received a subcutaneous injection of 2% Pantopon solution in a dose of 0.1 mg/kg body weight. Heparin was used as anticoagulant. Before cooling began, a 0.2% Nembutal solution was administered at intervals by intravenous drip until the onset of "cold anesthesia." The animals were cooled in an ice bath. As the body temperature fell and breathing was disturbed, artificial respiration was applied. If fibrillation developed it was arrested by single electric shock; asystole was treated by electrical stimulation of the heart. When the rectal temperature reached 20-23°C bleeding from the femoral artery was started, and continued until the onset of clinical death. The duration of clinical death was 2 hr. Resuscitation measures included intra-arterial blood transfusion, mechanical artificial respiration, defibrillation and electrical stimulation of the heart. To reverse the hypothermia, besides the general application of heat, an artificial circulation was provided by the centripetal injection of warm, aerated blood into the femoral artery and the simultaneous withdrawal of blood from the femoral or jugular vein. Active heating was discontinued when the body temperature reached 32°C. The blood to be injected was aerated by the oxygenator of the perfusion apparatus. In some experiments venous blood obtained from the experimental animal was injected into a donor for the purpose of oxygenation. Exchange transfusion was performed on some of the animals in the recovery period by the method of Glozman and Kasatkina (2). The ECG was recorded throughout the experiment.

RESULTS

As body temperature fell, the functions of respiration and the circulation were considerably modified. Besides a slowing of respiration, a gradual slowing of atrioventricular conduction took place, accompanied by a corresponding slowing of the heart rate. In some animals the shape of the ventricular complexes became disturbed at 28-26° C, as shown by the appearance of Osborne's waves, depression of the S-T segment and enlargement (or, less frequently, lowering) of the T wave on the ECG. At a body temperature of 26-21° C, single or grouped extrasystoles developed in 12 of the 31 animals, changing to ventricular fibrillation. Fibrillation during cooling lasted for between 30 sec and 25 min. At a low body temperature ventricular fibrillation, if it arose, was difficult to control by treatment. In 8 of 12 dogs, for instance, fibrillation could not be permanently controlled during cooling, and bleeding was started while the animal was having periodic attacks of ventricular fibrillation. Sixteen dogs did not fibrillate during cooling, and four fibrillated during exsanguination. Asystole was recorded in 2 of the 16 dogs during bleeding.

With an adequate depth of anesthesia, cooling took place more rapidly and fibrillation was less common. Only 6 of 20 dogs whose body temperature was lowered to 23-21° C over a period of 1-2 hr developed fibrillation. When the body temperature was lowered more slowly—over 2-5 hr—6 of the 11 animals developed fibrillation.

The onset of fibrillation was accompanied by respiratory disturbances, and artificial respiration was necessary. Artificial respiration also had to be applied on some animals which did not fibrillate, but developed respiratory disturbances during cooling. The timely application of artificial respiration prevented the development of ventricular fibrillation during cooling. This agrees with the observations of other authors (16, 17).

At the beginning of exsanguination the body temperature of the animals fell to 23-20° C. The period of clinical death lasted for 4-42 min. As bleeding continued and the temperature fell, the disturbances of pacemaker activity and conduction in the heart progressed. The terminal activity of the heart usually ended in fibrillation. More rarely, monophasic complexes of low amplitude could be observed for an hour after the onset of clinical death. At the beginning of the period of active resuscitation, the body temperature of the animals was 7.5-13° C.

Because of differences in the technique of restoration of the cardiac activity, for the part of the experiment including the resuscitation period the animals were divided into two groups.

In the first group (23 dogs) the venous system was drained via the femoral vein during perfusion, and the first intra-arterial transfusion consisted of blood taken

from the same animal during exsanguination. In the animals of the second group (eight dogs) continuous perfusion was maintained by intra-arterial injection of fresh donor's blood from two bottles at a time, and blood was withdrawn from the jugular vein during perfusion. Blood taken from the experimental animals during exsanguination was not susequently reinjected.

In both groups of animals when intra-arterial blood transfusion had continued for 2-6 min the electrical activity of the heart began to reappear, in the form of low-amplitude, fibrillary oscillations with a slow rhythm. An increase in the frequency of the fibrillary oscillations to 300-400/min and an increase in their amplitude to 0.5 mv were signs of restoration of myocardial function and of the possibility of effective defibrillation. In 13 of the 23 dogs of the first group the first cardiac contractions appeared after a period of 2.5-12 min, when the temperature was 12-18° C. Periodic interruptions of the cardiac activity, observed after restoration of the first contractions, were caused either by the onset of fibrillation or by the development of partial or complete atrioventricular block, for which defibrillation or electrical stimulation of the heart was necessary.

Delay in the initial part of the ventricular complex, together with distortions of its shape as a result of a right or left bundle branch block, were observed at this period. Conduction in the terminal branches of the conducting system was usually disturbed.

Only in one dog was stable cardiac activity restored quickly (after 150 sec), and in the other animals this took longer (after 12-72 min), after repeated defibrillation and electrical stimulation, while in two cases direct cardiac massage had to be used. Complete restoration of pacemaker activity took place in most animals when the body temperature had risen to 26-29° C at the 40th-70th minute of cooling. For a long period after restoration of pacemaker activity, conduction disturbances were observed in the myocardium of the right ventricle (a deep, wide S wave).

During resuscitation and recovery from deep hypothermia the animals received epinephrine to strengthen existing fibrillations and change them to strong contractions. The vascular tone of most dogs during resuscitation was extremely unstable and sharp fluctuations of arterial pressure were observed, while some dogs developed atrioventricular block. These animals were given intra-arterial or intravenous injections of small volumes of blood, glucose or polyglucin with epinephrine, norepinephrine and ephedrine periodically for long periods of time (2-3 hr or, in one case, for about 24 hr). When necessary the heart was stimulated electrically.

Cardiac activity could not be restored in the remaining 10 dogs of the first group because of acute dilatation of the heart as a result of faulty perfusion, and weak ventricular fibrillation persisted. In the later stages of resuscitation, all these dogs received direct or indirect cardiac massage in addition to intra-arterial injections. In some animals of this group fibrillation was difficult to stop not only because of acute dilatation of the heart, but also because overheated blood was used for perfusion, and this caused a thermal contracture of the heart muscle and thrombosis of the auricles of the atria. The resuscitated animals recovered their respiration after periods of 20-57 min at 18-27° C. In some dogs breathing returned while the heart was still fibrillating. The corneal reflexes returned after periods of between 57 min and 3 hr 32 min, at 26-33.2° C. Five of the 13 resuscitated dogs survived, of which three appeared outwardly to have recovered completely after periods of between 12 days and 3 months, and two showed signs of cerebellar disorders before they were sacrificed, 4-5 months and 1 year 3 months 10 days, respectively, after clinical death. Seven of the remaining eight resuscitated dogs died 1-2 days after the beginning of resuscitation. Postmortem examination of these animals revealed marked engorgement of the venous system, with multiple and, in some cases, extensive hemorrhages into the heart muscle and other organs. Some animals showed pulmonary edema and degenerative changes in the liver and kidneys (Romanova).

The experiments with the first group of animals disclosed various factors interfering with resuscitation: prolonged cooling of the animals and faulty anesthesia, leading to the more frequent development of ventricular fibrillation; acute dilatation of the heart, maintaining weak ventricular fibrillation, which was difficult to control; and in some cases asystole, developing at the beginning of resuscitation, when the venous outflow was insufficient during perfusion; finally, the use of inadequately aerated, overheated, or too cold blood for perfusion of the heart during resuscitation, or faulty perfusion technique during resuscitation, leading to long periods of depression of the arterial pressure below the critical level (60 mm).

Severe hemodynamic disturbances in the resuscitated dogs during the recovery period and severe metabolic acidosis continuing for several hours (according to Bulanova) during recovery from hypothermia also delayed the subsequent course of resuscitation and led to serious abnormalities of the internal organs and brain.

The object of experiments with the animals of the second group was to overcome these factors by the more active withdrawal of blood from the venous system during resuscitation, the provision of continuous transfusion, the intra-arterial injection of fresh donor's blood, and the use of exchange transfusion in the later stages.

As in the animals of the first group, at the beginning of resuscitation ventricular fibrillation developed in all eight dogs of this group. The first active contractions appeared in seven dogs after intervals of between 4 and 9 min at 13.5-16° C. In these animals, in contrast to the animals of the first group, brisk fibrillation developed, and was easily and quickly abolished. Electrical stimulation was used together with defibrillation in three of the seven dogs. The arterial pressure in five of the seven animals of this group was maintained above the critical level during perfusion, i.e., until the cardiac activity had been permanently restored, which occurred after 8-35 min. Indirect cardiac massage was necessary for one of these dogs. The vascular tone of most of the animals was stable after permanent restoration of the cardiac activity 40-60 min after the beginning of resuscitation. The general course of the ECG changes in the recovery period was similar to that observed in the animals of the first group, although the normal ECG was restored sooner and at a lower temperature.

In seven of the eight dogs of this group respiration was restored after 17-38 min at 18-23.5° C, and in one dog at the 98th minute of resuscitation, at 33.2° C.

The corneal reflexes were restored after 36-76 min at 21.5-32.4° C.

To hasten the subsequent resuscitation of the animals exchange trasfusions were performed on six of the eight dogs after restoration of their normal vascular tone 70-80 min after the beginning of resuscitation. Complete recovery of the vital functions took place in five of the eight dogs after a period of between 4 days and 1 month 7 days. In all these animals resuscitation began with perfusion of fresh donor's blood, and in addition, three animals also received exchange transfusion.

Three of the resuscitated dogs died on the first and second days: one from hemothorax and two from cardiac weakness. Two animals of the second group apparently died from severe hypoxia, arising during the first 40 min of resuscitation as a result of a faulty perfusion technique, in association with the rising temperature. The low arterial pressure, alternation of fibrillation with periods of asystole, and disturbances of cardiac rhythm in the later stages of resuscitation led to severe and irreparable changes in the heart, which were the immediate cause of death of the animals as a result of massive hemorrhages into the internal organs.

Comparison of the results of the experiments with the two groups of animals shows that the better the perfusion technique in the initial stages of resuscitation, the more easily cardiac activity is restored.

Exchange blood transfusion hastens the course of recovery. It can be concluded that a faster cooling technique, the correct choice of anesthetic and perfection of the perfusion technique during resuscitation will assist towards the prevention of the complications arising during resuscitation and the recovery period, and thereby enable successful resuscitation to be undertaken even after periods of clinical death exceeding 2 hr in duration.

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