RESUSCITATION OF ANIMALS AFTER LONG PERIODS OF CLINICAL DEATH DURING ISOLATED COOLING OF THE BRAIN

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Considerable attention has recently been paid by research workers to the method of isolated brain cooling. This type of cooling lowers the temperature of the brain selectively, and leaves the temperature of the rest of the body relatively high. According to some writers [3, 7, 8, 9] it is this factor which contributes to the prevention of those menacing phenomena of circulatory disorder frequently arising during cooling of the whole body. The low temperature of the brain enables it to be excluded from the circulation for fairly long periods of time without the risk of after-effects detrimental to the body as a whole [4, 10-13].

In our previous investigations [6] we showed that during general cooling, associated with a sharp decrease in the body temperature (26-20°), animals in the recovery period after clinical death lasting from 30 min to 1 h repeatedly developed ventricular fubrillation. Because of this discovery, we suggested that if the body temperature were kept higher than the brain temperature, the activity of the heart would be restored much more easily in animals after long periods of clinical death. This problem is considered in the present paper.

EXPERIMENTAL METHOD

Experiments were carried out on 15 dogs of both sexes weighing from 9.3 to 16 kg. Before the experiment, the animals were given a subcutaneous injection of 0.1 mg of 2% pantopon and 0.1 mg of 0.1% atropine solution per 1 kg body weight. Heparin was given to stabilize the blood.. Both carotid arteries and the femoral arteries and veins were exposed under local anesthesia. Cannulas connected to a coil immersed in an ice bath were inserted into the peripheral and central ends of the divided left carotid artery. Blood from the central part of the artery entered an ampule, from which it passed at a pressure of 80-100 mm Hg through the coil to the brain. During cooling, a clamp was applied to the right carotid artery. Before cooling began, and at intervals during its course, a 0.2% solution of nembutal was infused by intravenous drip.

In order to measure the brain temperature, a thermocouple was inserted into the brain tissue of eight dogs through a burr hole; sometimes the thermocouple was placed on the dura mater. The rectal temperature of all the dogs was taken at the same time. When the rectal temperature fell to 32.9-29.5°, blood was taken from the femoral artery until a state of clinical death developed.

Resuscitation was carried out by means of intra-arterial blood transfusion and artificial respiration, using a positive pressure apparatus. If fibrillation developed it was arrested by a single discharge from a condenser. During the experiment the respiration, the arterial pressure, and the ECG were recorded.

EXPERIMENTAL RESULTS

The experimental animals were divided into two groups: animals in which clinical death lasted 30 min (9 dogs) and those in which it lasted 60 min (6 dogs).

In most animals exsanguination was carried out between 52 and 85 min after the beginning of isolated cooling of the brain, when the body temperature of the dogs corresponded to moderate hypothermia (29.5-32.9°). The brain temperature at the moment of exsanguination had fallen to 27-24.3°, i.e., it was 4.0-8.6° lower than the rectal

temperature. The arterial pressure before exsanguination varied between the limits of 74 and 176 mm Hg, and the pulse rate was 82-136 per min. The respiration became slower as the temperature fell, and its rate at the beginning of exsanguination was 4-13 inspirations per min.

The time taken for death to ensue lasted from 8 min 20 sec to 24 min. During this period various disturbances of conduction and automatic activity characteristic of increasing anoxia were recorded on the ECG (incomplete and complete block of conduction, changes in the first and last part of the ventricular complex). These changes were similar to those reported by other writers [1, 5]. After the 20th-30th min of clinical death all signs of electrical activity of the heart vanished. At the conclusion of the period of clinical death, i.e., before the onset of resuscitation, the body temperature of the first and second groups of animals was almost the same as before exsanguination. The brain temperature of most of the dogs was between 0.3° and 3.0° lower, i.e., between 22° and 25.4°. During isolated cooling of the brain the first signs of electrical activity of the heart appeared in most dogs in the form of low fibrillary oscillations, and the amplitude of these waves increased as the anoxia progressively diminished.

The cardiac activity of 7 of the 9 dogs withstanding clinical death for 30 min was restored after an interval of 1 min 3 sec to 2 min 35 sec. The later restoration of the activity of the heart was associated with the onset of ventricular fibrillation at the beginning of resuscitation. In one of these dogs the cardiac activity which reappeared after 1 min 47 sec was immediately extinguished, and was not restored again until 21 min 35 sec after the beginning of resuscitation when direct cardiac massage had been used. In the two remaining dogs, in which fibrillation did not develop, the cardiac activity was restored rapidly—26 and 47 sec respectively after the beginning of intra-arterial blood transfusion.

Of the six animals withstanding clinical death for 60 min, permanent restoration of the cardiac activity was obtained in only four dogs at intervals of 1 min 42 sec to 3 min 33 sec after repeated defibrillation. In two dogs the fibrillation could not be arrested. The sluggish cardiac contractions developing in one of them 19 min 20 sec after the onset of resuscitation with the application of direct cardiac massage in conjunction with intra-arterial transfusion soon disappeared.

The ECG of the dogs immediately after resuscitation most frequently revealed heterotopic automatism, later changing to sinus automatism. Migration of a focus of automatism and polytopic extrasystoles were also frequently observed.

It is interesting that ventricular fibrillation developed during restoration of the cardiac activity in 13 of 15 dogs with isolated cooling of the brain, compared with 15 of 17 animals with general hypothermia and withstanding clinical death for the same length of time [6]. The incidence of fibrillation was thus the same in each case. Whereas the onset of fibrillation in the animals subjected to total hypothermia was associated with the sharp fall in the body temperature (25-18°), in the dogs with isolated cooling of the brain it was evidently due to the severity of the anoxia in relation to the fairly high body temperature (30-32°). This was confirmed by the experiments on the second group of dogs in which fibrillation developed not only during restoration of the cardiac activity, but also (in contrast to the animals of the first group) on many occasions after its restoration, and in two dogs it could not be arrested.

Respiration was restored in the resuscitated animals of the first and second groups of experiments after intervals of 5 min to 34 min 30 sec. The brain temperature at this time had risen to 28.2-30.8°, i.e., 0.8-1.7° below the body temperature. In 8 of the 9 dogs of the first group the corneal reflexes were restored after intervals of 17 min to 79 min 20 sec, but in one animal restoration of the reflexes did not take place. These reflexes returned in only one of the 4 resuscitated dogs of the second group, 103 min after the beginning of resuscitation.

Of the 9 dogs surviving clinical death for 30 min, the vital functions of three were completely restored on the 2nd and 8th days, and three surviving dogs died during the first 24 h. The condition of these animals was extremely grave before death took place: they did not react to their surroundings and could neither hear nor see. One animal regained its hearing at the end of the first 24 h, but paralysis of the hind limbs was observed. On the 5th day the dog began to see, but paresis of the hind limbs was still marked. Difficulty in breathing and cough soon developed. Despite antibiotic therapy, the animal died on the 15th day from bilateral pneumonia. Finally, two dogs died on the 1st and 5th days from brain trauma during insertion of the thermocouple: one from massive hemorrhage into the left cerebral hemisphere at the site of insertion of the thermocouple, and the other from compression of the brain by a hematoma.

Of the six dogs withstanding clinical death for 60 min, two could not be revived, two died on the 1st day (the higher divisions of the brain never recovered) and two died on the 1st and 11th days as a result of brain trauma (at necropsy on one animal an extensive subdural hematoma and cerebral edema were discovered, while the other gradually developed a brain abscess, which ruptured into the lateral ventricle).

As the postmortem findings showed, all the animals of both groups in which the cardiac activity and respiration were not restored, and also those dying during the first 24 h after the beginning of resuscitation were obviously not viable. Besides congestive hyperemia of the brain and the abdominal organs, extensive multiple hemorrhages were found in the substance of the heart muscle, the stomach, and the intestines. In addition to these changes, in one animal edema of the lungs and thrombosis of the right auricle of the heart were observed.

It is interesting to note that much better results were obtained in animals withstanding the same periods of clinical death as in our experiments, but during general hypothermia [6]. For instance, in the case of animals withstanding clinical death for 30 min during isolated cooling of the brain, two dogs died from brain trauma, and of the remaining seven, complete restoration of the fundamental vital functions took place in only three, and in one of them, moreover, this did not happen until the 8th day. In the case of animals exposed to general hypothermia, in 8 of the 10 dogs complete and rapid (on the 1st-4th day) recovery took place, and the other two died as a result of intensive and prolonged heating. Complete recovery was not observed in any animal subjected to clinical death for 60 min during isolated cooling of the brain;* on the other hand, 4 of the 7 dogs subjected to general hypothermia made a complete recovery.

Hence the pattern of recovery of the fundamental vital functions (cardiac activity, respiration) of animals exposed to clinical death for 30 min during isolated cooling of the brain showed no significant difference from the results obtained during general hypothermia. However, the subsequent course of recovery in these animals, and more especially in those subjected to clinical death for 60 min, was far less smooth than after general hypothermia. A possible explanation of this finding is the accumulation of incompletely oxidized products of metabolism during the prolonged, severe anoxia in association with the high body temperature, which adversely affects the subsequent process of restoration of the vital functions of the resuscitated animals. Furthermore, as the postmortem findings showed, severe anoxia in these conditions leads to a sharp increase in the permeability of the blood vessels, which in a large proportion of cases was the direct cause of death of the animals as a result of massive hemorrhages into the internal organs.

We cannot ignore the statements made by other writers [2, 9] that after isolated cooling of the brain, unaccompanied by any other procedure, many of the dying animals show considerable changes in the nerve cells of the brain, resulting from the disturbance of the normal cerebral circulation by the artificial perfusion.

SUMMARY

A study was made of the possibility of restoring the vital functions in dogs following prolonged periods of clinical death in conditions of isolated cooling of the brain. As established, dynamics of the restoration of cardiac activity and respiration in animals after a 30 min clinical death in isolated cooling of the brain (body temperature 32.9°C to 29.5°C, brain temperature from 4 to 8.6°C lower) did not differ materially from the results obtained with the general body chilling. However, subsequent restoration in these animals (especially after one hour of clinical death) occurs with much greater difficulty than following general chilling. This may be attributed to the accumulation of suboxidized metabolites in the body during prolonged severe hypoxia in conditions of high body temperature, these metabolites exerting an unfavorable effect on the subsequent restoration process in revived animals. Along with this, as shown by autopsy data, severe hypoxia in such conditions leads to a marked rise in vascular permeability, which in a great proportion of the cases served as a direct cause of the animal's death as a result of massive hemorrhages into the internal organs.

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