PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

THE USE OF OXYGENATED BLOOD IN EXPERIMENTAL RESUSCITATION

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There are references in the literature to the desirability of saturating with oxygen blood that is to be fed intra-arterially in order to restore the function of individual organs or the organism as a whole [1, 2, 8, 14]. It is known that when blood is administered intra-arterially it by-passes the lesser circulation and passes directly into the blood vessels of vitally important organs which are particularly sensitive to hypoxia, whereas on being administered intravenously the blood passes through the lungs where it is saturated with oxygen prior to entering the greater circulation. In connection with this, the question of oxygenating blood to be given intra-arterially has acquired considerable importance. In the practice of blood transfusion two methods of blood oxygenation are known and have been applied: bubbling of pure oxygen through the blood and addition to it of 3% or 30% solution of hydrogen peroxide. A number of authors [1, 2, 3, 4, 9, 11] saturated blood to be used intra-arterially with oxygen by adding 0.5-1.0 ml 3% or 30% solution of hydrogen peroxide and observed favorable results. However, in recent years, greater and greater attention has been directed to oxygenation of blood to be given intra-arterially by passing through it pure oxygen under pressure [6, 7, 10, 12, 13, 15]. Special apparatuses are in use for this purpose in which oxygenation of the blood takes place both before and during its administration. It must be noted that these reports are based on small numbers of observations, and the questions concerning the most effective means of oxygenating blood as well as of the effect of oxygen-saturated blood on the restoration of vital functions of the organism remained insufficiently clarified. It appeared interesting in this connection to discover the relative effectiveness of combined methods of resuscitation with intra-arterial administration of nonoxygenated or oxygenated (by various methods) blood as regards the process of restoration of the vital functions of animals following clinical death produced by exsanguination.

EXPERIMENTAL METHODS

Forty experiments were performed on dogs. Following a preliminary subcutaneous injection of 2% solution of pantopon (8 mg per 1 kg body weight) the femoral vessels were dissected bilaterally under ether anesthesia. The left femoral artery was connected by a system of rubber tubes to a mercury manometer for recording of arterial blood pressure. Respiration was recorded by means of a cuff placed round the animal's thorax and connected to Marey's tambour. Arterial pressure and respiration were recorded on a kymograph. Exsanguination by way of the right femoral artery was performed after preliminary administration of heparin. The amount of blood drained consituted 62%, on the average, of the total volume of blood if it is taken that the total amount of blood equals 9.2% of the total body weight. Restoration of vital functions began 5-7 minutes after onset of clinical death. The technique has been developed by Professor V. A. Negovsky and his collaborators. The method consists essentially of centripetal feeding of blood into the artery and simultaneous application of artificial respiration by means of apparatus which blows air into the lungs. Oxygenation of the blood was effected in 17 experiments by addition of 2.0 ml 3% solution of hydrogen peroxide per 300-400 ml blood. Hydrogen peroxide was placed in the bottom of the flask together with glucose (0.5 g 40% solution per 1 kg body weight), the flask was then filled with blood, with shaking. The blood usually acquired a bright color during this procedure. In 8 experiments the blood was oxygenated by means of a jet of oxygen from a cylinder, under pressure of 250 mm Hg. At the moment of intra-arterial introduction the escape of oxygen from the flask was stopped and a positive pressure (which could be regulated) of oxygen on blood was created; the blood entered the artery under this pressure. In a number of experiments the degree of oxygen saturation of arterial blood was determined, using the Kipp hemioreflector, at different stages of dying and resuscitation. The same method was used to determine the oxygen saturation of the blood drained from the animal before and after oxygenation of this blood.

EXPERIMENTAL RESULTS

Three series of experiments were carried out. In the first series (17 experiments oxygenation of the blood to be administered was effected by the addition of 2.0 ml 3% solution of hydrogen peroxide (freshly prepared) per 300-400 ml of blood. This led to an increase in oxygen saturation of blood in the flask from 85-95% to 90-98%. The period of dying in most animals of this series (9 of 17) lasted from 6 minutes 24 seconds to 9 minutes 48 seconds, in 5 animals this period was of medium duration – from 10 minutes 10 seconds to 14 minutes 35 seconds – in 2 animals it was prolonged – 21 minutes 28 seconds and 22 minutes 48 seconds. Duration of clinical death in the animals in 10 experiments was from 4 minutes 54 seconds to 5 minutes 10 seconds and in 7 experiments – from 7 to 8 minutes.

Cardiac activity was restored in most experiments (6 of 10) after 5 minutes of clinical death 20-27 seconds following the beginning of resuscitation, in 3 experiments following 32-35 seconds and in one experiment (Experiment 1) following 12 seconds. In the majority of experiments (5 out of 7) cardiac activity was restored after 30-34 seconds in animals which had sustained clinical death lasting 7 minutes, and 2 experiments it was restored 42 and 54 seconds after beginning resuscitation.

Restoration of respiration in animals which had sustained clinical death lasting 5 minutes occurred after 1 minute 36 seconds – 2 minutes 56 seconds from the beginning of resuscitation. Experiments 6 and 7 were exceptional in that the period of dying was prolonged (14 minutes 35 seconds and 22 minutes 48 seconds) and respiration in these animals was restored after 4 minutes 33 seconds and 7 minutes from the beginning of resuscitation. Restoration of corneal reflexes in most animals after 5 minutes of clinical death occurred after 10 minutes 40 seconds – 16 minutes, in 2 experiments after 7 minutes 24 seconds and 7 minutes 20 seconds and in one experiment in which restoration of respiration was delayed the corneal reflexes appeared 20 minutes 12 seconds after the beginning of resuscitation.

Spontaneous respiration in animals which had sustained clinical death lasting 7 minutes was resumed 1 minutes 42 seconds – 4 minutes 54 seconds from the beginning of resuscitation. In one experiment the animal's respiration was restored after 6 minutes 40 seconds; this was connected with hyperventilation and damage of pulmonary tissue during artificial respiration. The corneal reflexes in most animals appeared 15 minutes 6 seconds – 23 minutes 36 seconds, in 2 experiments 10 minutes 12 seconds and 9 minutes 6 seconds after the beginning of resuscitation.

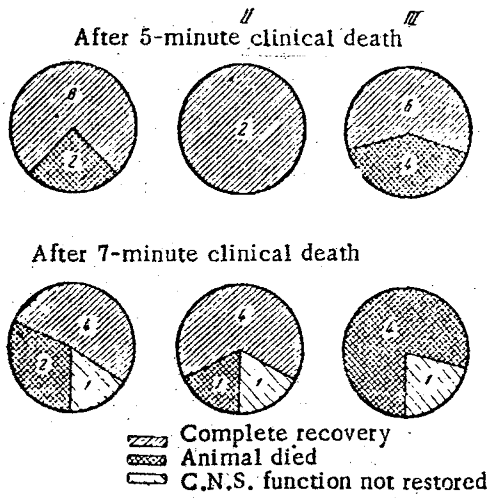
Restoration of central nervous system function occurred in 8 out of 10 animals subjected to clinical death lasting 5 minutes. Complete restoration of vital functions in most of the animals in this group occurred 36-60 hours after the experiment. Complete recovery of the animals was judged only by their outward behavior. No conditioned reflex studies of higher nervous activity were carried out. Of the 7 animals subjected to 7-minute clinical death 2 died soon after the experiment while 5 survived; in 4 of these central nervous system function recovered but in one the recovery was partial, since neither vision nor hearing was restored.

In the second series (8 experiments) oxygenation of the blood to be administered intra-arterially was effected by passing through it a jet of oxygen from a cylinder under pressure (250 mm Hg) at the rate of 600 ml/min Oxygenation of the blood was started 10-15 minutes before resuscitation, the oxygen saturation of the blood rising during this period from 82-94 to 96-97%. The blood was fed into the artery under the pressure of oxygen. The period of dying in this series varied from 8 minutes 10 seconds to 16 minutes 52 seconds. Clinical death lasted 5 minutes 21 seconds and 5 minutes 3 seconds in 2 experiments and from 7 to 7 minutes 5 seconds in the remaining 6 experiments. Cardiac activity was restored in most of the animals in this series 45 seconds – 1 minute 15 seconds and in one animal 35 seconds after the beginning of resuscitation. During the recovery of cardiac activity one animal developed fibrillation which was abolished by a condenser discharge, the cardiac activity being again restored 3 minutes 55 seconds from the beginning of resuscitation. The somewhat later restoration of cardiac activity in these experiments as compared with those of the previous series may be explained by the fact that the pressure necessary for administering the blood from the flask developed over a period of 40-50 seconds and during the initial stage of resuscitation the blood entered the artery under insufficient pressure. As has been shown by the work carried out in the laboratory (V. A. Negovsky, E. M. Smirenskaya) it is impossible to create the necessary level of circulation in the coronary vessels supplying the heart muscle when the pressure is insufficient.

Respiration was restored in 4 animals after 3 minutes 15 seconds – 4 minutes 18 seconds from the beginning of resuscitation. In 3 animals respirations appeared after 6 minutes 2 seconds – 6 minutes 35 seconds and in one animal after 2 minutes 20 seconds. Corneal reflexes were restored in the majority of animals 13 minutes 5 seconds – 16 minutes 45 seconds after the beginning of resuscitation, in 2 animals – after 18 minutes 35 seconds and 20 minutes 5 seconds. Subsequently, of the 8 animals in this series 7 survived and one died 24 hours after the experiment; complete recovery of functions occurred in 6 dogs, in 4 of these after 2-3 days, in 2 after 5 and 10 days following the experiment. Only partial recovery of central nervous system function took place in one animal; hearing and vision were not restored 2 weeks after the experiment.

The third series consisted of 15 control experiments in which nonoxygenated blood was used. In 10 experiments the duration of clinical death ranged from 4 minutes 54 seconds to 5 minutes 10 seconds, the period of dying lasting from 8 minutes 5 seconds to 17 minutes 55 seconds; in 5 experiments clinical death lasted 6 minutes 59 seconds – 7 minutes 9 seconds and the period of dying ranged from 6 minutes 6 seconds to 12 minutes 6 seconds. The amount of blood loss varied from 51 to 81% of the total amount of blood.

Cardiac activity in the animals whose clinical death lasted 5 minutes was restored after 27-42 seconds. Only in one experiment it was restored 1 minute 12 seconds from the beginning of resuscitation. Animals which had sustained 7-minute clinical death showed restoration of cardiac activity after 38-55 seconds. Respiration in the former group of animals was restored after 2 minutes 35 seconds – 3 minutes 50 seconds and in two animals after 7 minutes 16 seconds and 5 minutes 54 seconds from the beginning of resuscitation. In the case of the latter group, respiration was restored after 3 minutes 54 seconds – 8 minutes 30 seconds from the beginning of resuscitation. Corneal reflexes in animals whose clinical death lasted 5 minutes appeared after 12 minutes 20 seconds – 21 minutes 10 seconds and in one animal after 8 minutes 20 seconds. Of the 10 animals which sustained 5-minute clinical death 6 survived; of the 5 animals subjected to 7-minute clinical death one survived, but its vision failed to recover. The remaining animals died in the course of the first twenty-fou hours after the experiment.



Combined method of resuscitation of animals. I) Use of blood oxygenated by addition of 3% hydrogen peroxide solution; II) use of blood oxygenated by passage of a jet of oxygen under pressure; III) use of nonoxygenated blood.

It is well known that the time of restoration of cardiac activity, respiration and corneal reflexes are of great significance in the process of animal resuscitation. But the most important indication of the effectiveness of combined methods of resuscitation with intra-arterial administration of oxygenated or nonoxygenated blood is the restoration of C.N.S. function in the animal. Comparison of experimental results by stages of resuscitation reveals that animals resuscitated after 5 and 7-minute clinical death by intra-arterial administration of oxygenated blood show a tendency to accelerated restoration of cardiac activity, respiration and corneal reflexes. Thus, 9 out of 17 animals in the first series showed definite acceleration of recovery of cardiac activity as compared with control animals which sustained analogous periods of dying and clinical death. In 7 animals of the first series more rapid restoration of respiration and, in a number of experiments, of corneal reflexes were observed. The advantage of using oxygenated blood is however, most vividly demonstrated by a comparison of the results obtained in the 1st and 2nd series with those of the control experiments. As can be seen from the figure, the most favorable results were obtained in the first and second series of experiments, in which oxygenated blood was used. Of 12 animals which sustained 5-minute clinical death and were resuscitated by oxygenated blood, C.N.S. function was restored in 10 dogs, whereas of 10 control animals with analogous periods of dying and of clinical death complete recovery of function only occurred in 6 dogs. Of 13 animals which sustained 7-minute clinical death and were resuscitated by intra-arterial administration of oxygenated blood 10 survived, 8 with recovery of C.N.S. function, while of 5 control animals partial restoration of function was noted in only one dog. It must be mentioned that in the experiments of the second series complete restoration of vital functions occurred in the majority of animals (6 out of 8), despite delayed restoration of cardiac activity, and in some experiments of respiration as well, as the result of faulty technique.

The mechanism of the favorable effect of oxygenated blood on restoration of vital functions revealed in these experiments is not yet sufficiently clear. Although it may seem that the difference in the degree of oxygen saturation of the blood before and after its oxygenation is relatively small, in practice it exerted a definite effect on the physiologic results of the experiments. Apparently, the additional oxygenation of the blood, even though it did not result in a great difference in the level of saturation, exerted a significant effect on the increase of partial pressure of gaseous oxygen in the blood entering the artery. This would assist a somewhat more vigorous course of oxidative processes in the tissues which undoubtedly constitutes a positive factor in the course of subsequent restoration of the animal's vital functions. It must be pointed out that the favorable effect of increasing the partial pressure of oxygen on the restoration of cardiac activity has also been noted by V. S. Shapot and G. M. Pruss [5] and by some other authors.

The present experiments have thus demonstrated the positive effect produced by oxygenated blood on the process of restoration of the organism's vital functions. This allows the hypothesis that clinical use of oxygenated blood for intra-arterial administration may also be beneficial in the treatment of terminal conditions.

SUMMARY

The effect of blood (oxygenated by various methods) on the process of recovery of vital functions of the organism following clinical death caused by loss of blood was studied. It was established in experiments on dogs that the percentage of survival with complete recovery of the vital functions was much greater in animals which were treated by oxygenated blood in comparison with those which received ordinary blood.

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* In Russian.