

Prolonged Deep Hypothermia[®]

Report of a Case

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Abstract

Observations made during and after prolonged deep hypothermia (7 hours between 6-20° C) are reported in a case operated for a rhinopharyngeal haemangioma with severe blood loss during cardiopulmonary bypass. Near normal numerical values of the acid-base parameters when corrected to the current temperature were aimed at. No organic damages could with certainty be described to the hypothermia itself or to the prolonged perfusion.

A case of prolonged, deep hypothermia during the application of cardiopulmonary bypass will be reported. For literature and for the theoretical background of using deep hypothermia the reader is referred to a review by I. H. Rygg (1969).

Case Report

A man, aged 34, had for the past 12 years had repeated, alarming haemorrhages from a rhinopharyngeal haemangioma. He had previously been treated with X-rays and with sclerosing injections as well as ligation of both external carotid arteries. Prior to his present admission he had been tracheostomized, since for long periods he had compressing packs in the nose and pharynx. In addition, gastrostomy was established for nourishment.

The operation was performed in October 1963 by a collaboration between oral surgeons, neurosurgeons, thoracic surgeons, and anaesthetists. The pharyngeal procedure was fairly extensive and was done by splitting both the upper and lower jaw. Both external carotid arteries were again ligated, and so was the left vertebral artery. To reduce the bleeding, the left common carotid was isolated and clamped during several phases of the operation. The operation was carried out under deep hypothermia with total circulatory arrest for 47 min. and "partial" circulatory arrest for 150 min. during

which a perfusion was kept up only at a blood flow rate of 1 liter/min. The deep hypothermia was performed by the aid of a Rygg/Kyvsgaard heart-lung machine* with heat exchangers inserted both in the arterial and the venous line. Cooling was done by recirculating ice-water. The heart-lung machine was connected through a median thoracotomy, int. al. because the innominate artery as well as the left carotid were to be isolated at the origin from the aortic arch. Catheters were inserted into both caval veins and suction applied in the left heart through the root of the right superior pulmonary vein.

During the operation the EEG, ECG, rectal temperature, the temperature of the mixed caval blood as well as the arterial and venous pressure were constantly recorded. In addition, the hourly urinary output was collected and blood samples were frequently drawn.

As it was not known beforehand how long the excision of the hemangioma would take, and thereby how long-lasting the total circulatory arrest had to be, it was decided to cool the patient to below 10° C. The cooling procedure took about 2 hours. Thereafter the circulation was totally arrested for three periods totalling 47 min. while the haemangioma was being excised. The first attempt at starting full perfusion again to rewarm the patient gave rise to profuse haemorrhage from the operative field. Since the field was infected, the blood could not be returned to the heart-lung machine, and a great blood loss was sustained. At the end of 45 min. therefore, he had to be cooled again to reduce the perfusion to a minimum, partly to obtain better haemostasis and partly to procure more donor blood. How-

*Incorporating a Rygg-Kyrsgaard Disposable Bubble Oxygenator. Polystan (Canada) LTD, 792 Kennedy Road, Scarborough, Ontario, Canada.

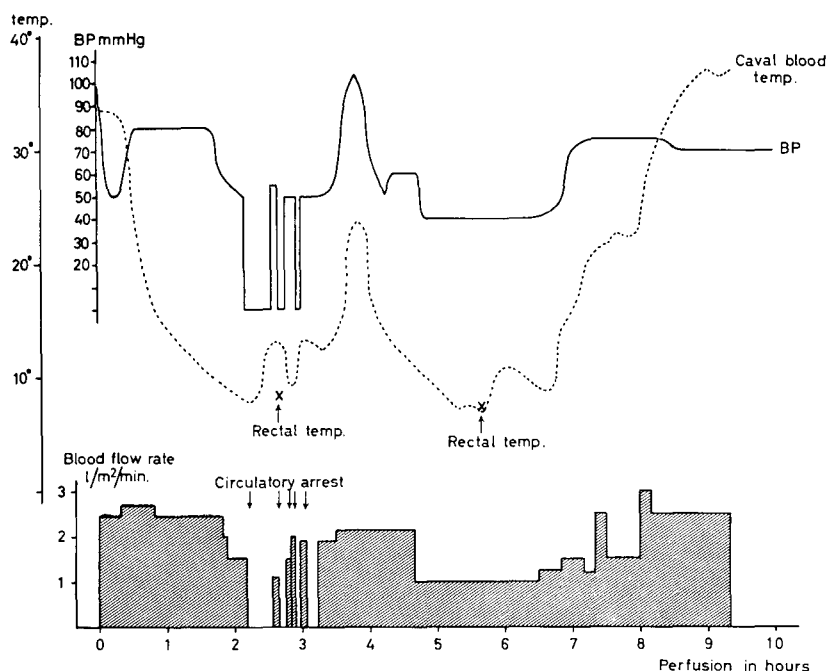


Fig. 1. Blood flow rate, arterial blood pressure and mixed venous temperature during the cardio-pulmonary by-pass and deep hypothermia.

ever, it was impossible to secure adequate haemostasis, so that a very tight compression by muscle and gauze was established in the operative field. After 2 hours of low-flow perfusion, the rewarming could be started, and this took another couple of hours. During this period, too, the flow had to be reduced, because of a great blood loss, in order to await further donor blood. After rewarming to a rectal temperature of 35° C, spontaneous sinus rhythm re-appeared. The perfusion was interrupted, and satisfactory haemostasis was obtained a short time after the heparin had been neutralized by protamine sulphate.

The heparinization was started by 3 mg/kg, and a supplement of 1 mg/kg was given every hour throughout the procedure. All the donor blood was drawn into polyethylene bags of 500 ml containing 25 mg heparin. A total of 95 portions of blood (47 liters) were used. The patient was perfused for a total of 9 hours; for 3 hours of this period the temperature was below 10° C, for 5 hours below 15°, and for 7 hours below 20° C. The lowest recorded temperature was 6.7° C in the caval blood.

Observations during the perfusion

The perfusion was started at a flow of about 2½ liters/m²/min, and this flow was, broadly speaking, maintained throughout the cooling period, with a mean B.P. of approx. 80 mm Hg. After the circulatory arrest, rewarming was first started at a somewhat lower flow rate of about 2 liters/m²/min. and during this period, which lasted for some 1½ hours, the B.P. was most of the time below 60 mm Hg. Thereafter, a very low flow was maintained for a couple of hours during the second period of deep hypothermia, and in this period the B.P. was maintained at only approx. 40 mm Hg. The venous pressure during this period was 3-5 mm Hg, while in periods with a higher flow it rose to about 10 mm Hg. During rewarming the flow was again increased to approx. 2½ liters/m²/min, corresponding to a total flow of about 4½ liters/min. During the rewarming period the mean B.P. was at about 70 mm Hg. After the perfusion, the patient very nicely kept up a spontaneous B.P. of approx. 130/80 mm Hg.

The hourly urinary output followed very closely the alterations in the B.P. During the first hour of cooling it was 25 ml, and during the next period, when the temperature in the mixed caval blood was below 15° C, it was 60 ml. Thereafter, no urine was produced during the circulatory arrest (4ml). After the rewarming period in the middle of the procedure only about 8 ml urine was produced, and during the 2-hour period of a low flow and low B.P. the hourly output was from 0-3 ml. Thus, during a total period of 6 hours only about 17 ml urine was produced. During the rewarming period, when the B.P. rose to 79 mm Hg, the urinary output again increased to 24 ml/hour and in the subsequent hours the hourly output rose to 150 ml.

The temperature was measured in the mixed caval blood as well as in the rectum. During the most rapid part of cooling, there was quite a considerable gradient of up to 10° C between these temperatures. At temperatures below 10° C, the gradient was less than 1½° C. During the brief rewarming in the middle of the hypothermic period the temperature in the caval blood rose to 24° X, while the rectal temperature reached only 18° C. During the subsequent cooling the two temperatures again approached each other. During the circulatory arrest performed as an intermittent arrest—of 25, 7, 1, 4, and 10 minutes' duration—the temperature of the caval blood rose from 7.8° C to 11.4° C, and the rectal temperature from 8.9° C to 11.8° C. During the second period of deep cooling the temperature in the caval blood was as low as 6.7° C and in the rectum 7.2° C.

In respect to the cardio-respiratory function it may be mentioned that ventricular fibrillation occurred when the caval blood got below 25° C. Below 10° C there was apparently asystolia, while during rewarming there was again vivid fibrillation which spontaneously passed into sinus rhythm at 35° C. During the brief rewarming in the middle of the procedure as well as during the final rewarming, spontaneous respiratory movements started at a caval-blood temperature of 14-15° C. At above 20° C there was regular, spontaneous respiration. The cardiac action and respiration remained unchanged and

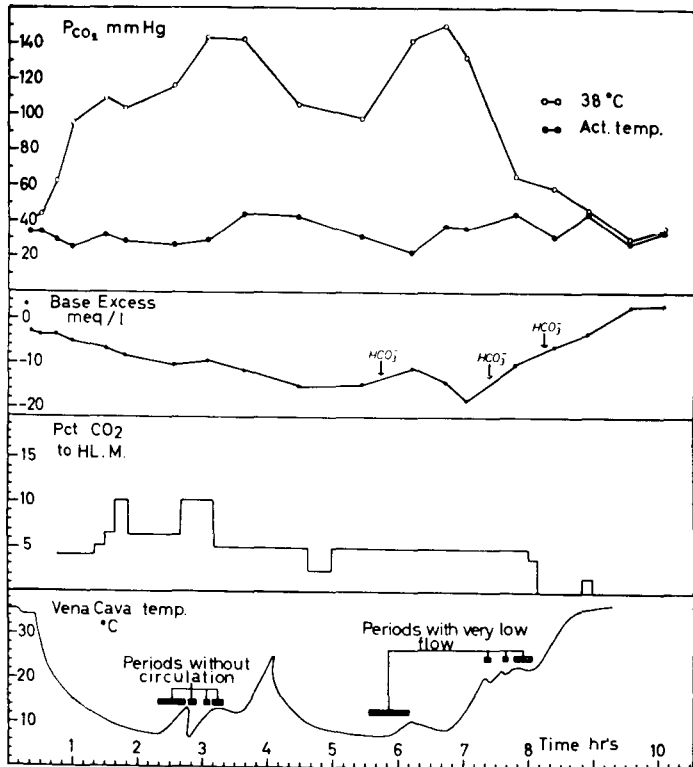


Fig. 2. Carbon dioxide tension at 38°C and at the actual temperature during hypothermia. Base deficit during the procedure. Percentage of CO₂ added to oxygen for ventila-

adequate after the operation which lasted for a total of 16 hours.

The acid-base balance exhibited several interesting alterations in the course of the hypothermia. As already mentioned frequent blood samples were drawn from the brachial artery and analysed for pH, PCO₂, standard bicarbonate, base excess, and oxygen saturation. Arterial oxygen saturation was around 100% throughout, also during the rewarming period. The ventilation in the oxygenator consisted of oxygen and carbon dioxide, a total of 5 liters/min. The carbon dioxide percentage was regulated according to the analyses of PCO₂ in arterial blood. These analyses were done at two temperatures and corrected to the current temperature in the caval blood at the time of sampling. At the beginning of perfusion the PCO₂ was 34 mm Hg. During the cooling 5% CO₂ was administered at the outset, but the tension in the arterial blood fell to 23 mm Hg, so that the CO₂ admixture to the oxygen used for ventilation had to be increased as far as 10% for a total period of 1 hour during the cooling period in order to maintain the PCO₂ level of the blood. Nevertheless, the PCO₂ did not exceed 30 mm Hg at the current temperature. During the periods of circulatory arrest the PCO₂ remained at this low level, while it rose to above 40 mm Hg during the brief rewarming period when the CO₂ percentage was temporarily reduced to 2.5%. During the second period of deep hypothermia 5% CO₂ was administered continuously, but in spite of the low minute volume of 1 liter/min used during this period the CO₂ tension in the arterial blood dropped to below 30 mm Hg. During the rewarming period 5% CO₂ was administered constantly up to a temperature of approx. 20°C while administration of pure oxygen was required during the remainder of the rewarming procedure to keep the CO₂ tension below 40 mm Hg. In blood analyzed at

38°C (the temperature generally used in stating the acid-base balance according to Siggaard-Andersen & Astrup's diagrams) the PCO₂ values were very high, even exceeding 140° mm Hg. The maximum values were found after resumption of full circulation when the rewarming period was started.

During the period of cooling accumulation of acid (non-respiratory) was apt to occur, manifesting itself as a fall in base excess of approx. 6 mEq/l. When circulation was resumed after the total circulatory arrest, a further fall of similar magnitude occurred, and this fall was only partially corrected for by administration of NaHCO₃ during the second period of hypothermia. When full circulation was resumed after this period, there occurred a pronounced fall, to a level of -19 mEq/l. This was corrected for by administering bicarbonate, and the correction thereafter continued spontaneously up to an excess of base, manifesting itself in a positive base excess at the conclusion of the perfusion.

Coagulation also showed marked deviations. The degree of heparinization was far greater than normal, but (incidentally) fluctuated widely. As already mentioned, large quantities of freshly drawn donor blood were given. Fibrinogen and plasminogen fell, and the platelet count dropped to values between 50,000 and 100,000. Fibrinolytic activity, measured at 37°C, was greatly increased during the period of hypothermia, but fell during rewarming and returned to normal immediately after the perfusion. The platelet count showed an increase during the rewarming period in the course of which numerous portions of fresh blood were given. After cessation of the perfusion protamine sulphate was administered, and this was immediately followed by normal coagulation and adequate haemostasis.

To assess organ damage, during the perfusion, determination of the tissue enzymes glutamate-oxalate-transaminase, glutamate-pyruvate-transaminase, and lactate dehydrogenase (LDH) was performed. The last-mentioned determination was, moreover, supplemented by determination of LDH isoenzymes. Before the perfusion these enzymes proved to be normal. In the course of the perfusion there was an increase of the isoenzymes in fractions 2, 3, 4, and 5 as well as of LDH to 50 units/ml. After the perfusion had been concluded all the enzymes were near-normal, but during the subsequent 3 days the LDH rose, and investigation of the LDH isoenzymes showed, on the second day, an increase of all five fractions; in particular, the increase of 5 suggested liver damage.

As mentioned above, the perfusion was carried out by the Rygg/Kyvsgaard heart-lung machine using a disposable bubble oxygenator. No technical difficulties were experienced during the perfusion. The same oxygenator was used all the time, defoaming was entirely sufficient, and examination after the perfusion showed surprisingly little deposition of fibrin in the defoaming fibres and very little deposition in the filters. The perfusion lasted for some 9 hours, apart from the circulatory arrest of 47 min. For about 6 hours of this period the perfusion was kept at or above a flow of 4 l/min.

Postoperative course

At the completion of the operation the temperature was only 35°C, and artificial ventilation was continued; as mentioned above, the patient already had a tracheostomy. About 2 hours after the operation the patient responded when addressed by opening his eyes and moving his hands. Four hours after the operation the temperature was 36°C, and breathing was regular, but somewhat laboured. At this stage he had a short-lasting tonic seizure, of a few seconds' duration, with

dilated pupils and gaze deviation to the right. It was decided, therefore, to keep up artificial ventilation, and the patient spent the next 3 weeks in a respirator. There were no further seizures. The patient was treated with phenytoin, phenobarbitone, and chlorpromazine, and received pethidine for pain. Compressing gauze had been applied to the rhinopharynx and mouth, but at the examination 3 days after the operation the patient could be described as fully oriented and awake, could make himself understood by movements of the mouth, and he moved all four limbs. However, there were signs of mild right-sided hemiparesis with exaggerated reflexes in the right leg 2 weeks after the operation. The EEG was severely abnormal 12 days after the operation, but steadily improved, and had returned to normal on the 12th postoperative day. During the postoperative course there was infection of the rhinopharynx, as the dressing was left for 10 days; at the same time some pulmonary infiltrations appeared. The infection subsided after removal of the pack and administration of antibiotics, but it was accompanied by tachycardia up to 180, a fall of B.P., and cardiac failure. The patient received digitalis and quinidien. This episode lasted for one week. It was associated with hepatomegaly and an increase in serum bilirubin of 9-11 mg/100 ml. There had previously been an increase in serum bilirubin, about one month prior to the operation, in connection with haemorrhage and many transfusions. The serum bilirubin returned to normal in 4 weeks. There were no signs of damage to the kidneys or bone marrow, and the gastrointestinal function was unaffected. Convalescence was long, but 6 months after the operation the patient was again able to take over the management of his business. Five years after the operation he is in good health, with normal EEG, normal blood cell counts, normal electrolytes and normal kidney function.

Discussion

To our knowledge, this case represents one of the longest-lasting deep hypothermias ever done in clinical practice. During the hypothermia efforts were made to keep the acid-base balance at a level which was believed to be normal at the current temperature. Thus, it was attempted to keep the PCO_2 in the arterial blood at the current temperature at around 40 mm Hg. This was accomplished with fair success by using 10% carbon dioxide in the oxygenator during the cooling period. As this high content of carbon dioxide was maintained for about one hour, with a total gas flow of about 5 l/min in the oxygenator, it corresponds to dissolving 30-40 liters of carbon dioxide in the patient during the cooling period, in addition to the quantity of carbon dioxide produced in the body. This administration of carbon dioxide caused a marked fall in pH measured at 38°C, and the PH was further affected by the simultaneous metabolic acidosis. The lowest pH measured at 38°C was 6.79. The patient was cooled by recirculation of ice-water through two heat exchangers, contrary to the recommendations of most previous authors. The cooling phase from approx. 33° to approx. 12° C in the caval blood was only half an hour. This rapid cooling explains the necessity of adding 10% CO_2 to the oxygen used for the ventilation of the machine. In the event of slower cooling and smaller temperature gradients between caval blood and cooling water, it is seldom necessary to add more than 5% CO_2 . It cannot be said with certainty whether this rapid cooling was harmful. The blood circulation was good throughout the perfusion, with application of an unreduced, high blood flow rate during the cooling period.

Very mild metabolic acidosis arose during the cooling period. However, the acidosis increased considerably during the period of total circulatory arrest and during the period while the minute volume was kept at 1 liter/min. The acidosis did not really manifest itself until the perfusion was increased, presumably because this established blood circulation in areas which had not been perfused at the low flow. The development of metabolic acidosis shows that considerable metabolism takes place even at temperatures below 10°C.

It should be stressed that the acid-base balance in this case was more shifted towards the acid side than had been intended, as no correction was made for the metabolic acidosis until late in the perfusion. The pH at the current temperature was, therefore, as low as 7.25 during the last part of the deep hypothermia, and this cannot be said to be desirable.

There was no major gradient between the rectal temperature and the temperature of the caval blood during the deepest hypothermia. This may be interpreted to the effect that the temperature in the brain has not been much higher, as there is a fairly good correlation between the cerebral and rectal temperature. However, we do not know whether the cerebral blood supply has been entirely normal in this patient who had already had ligation of the vertebral artery and both external carotid arteries and whose left internal carotid artery had been clamped during several periods of the perfusion to reduce bleeding. The mild right-sided hemiparesis during the postoperative course is possibly explicable as a consequence of these clampings of the left internal carotid.

It cannot be said with certainty that any organs have been harmed by the hypothermia itself or by the perfusion. As already mentioned, the cerebral changes may be explained by the surgical procedure proper, and the changes found in the LDH isoenzymes may be explained by the large number of blood transfusions, although a very mild hepatic damage due to the perfusion cannot be ruled out. The isoenzymes returned to normal on the 4th and 5th postoperative day, but again became abnormal in connection with the cardiac failure from the 10th to the 15th postoperative day. As mentioned above, there were no definite signs of any other organ damage. The very mild changes in the clotting mechanism, where a greater fall in platelets and perhaps bleeding disturbances would have been expected postoperatively, may be explained by the good effect of the numerous transfusions of fresh donor blood.

It is worth noting that the perfusion was carried out with a disposable bubble oxygenator which functioned entirely satisfactorily throughout the long perfusion. However, the numerous transfusions considerably reduced the traumatic effect of the perfusion, while they made increased demands on defoaming and filtration.

REFERENCES

Rygg, I. H. 1969. Deep Hypothermia. A review and lines for application of deep hypothermia with cardiopulmonary bypass. *Acta Anaesth Scandinav.* (In press).

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Note: The editor's wish to thank Colin Green for his assistance in procuring this paper.