APPLICATION OF PULSATILE CARDIOPULMONARY BYPASS FOR PROFOND HYPOTHERMIA IN CARDIAC SURGERY*

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Profound hypothermia with core cooling has been considered unsafe as compared with surface cooling because of the induced metabolic acidosis. We carried out studies on mongrel dogs to determine whether or not conventional cardiopulmonary bypass with pulsatile blood flow for core cooling could replace the bypass with non-pulsatile flow. The recovery time from anoxic damage of the brain due to circulatory arrest was also studied.

Cerebral excess lactate (ΔXL) (Huckabee) was determined throughout the course of hypothermia. During the cooling period from 30°C down to 20°C, the mean value of ΔXL in the pulsatile group was significantly lower than that in the non-pulsatile group (p < 0.01). After forty minutes of the first total arrest at 20°C, thirty minutes of pulsatile perfusion tended to eliminate the anaerobic metabolism of the brain caused by the first total circulatory arrest (p < 0.1).

Thus, the anaerobic metabolism in the brain appears to be highly suppressed with pulsatile cardiopulmonary bypass during the cooling period. Correction of congenital heart disease in infancy can probably be more safely performed if pulsatile cardiopulmonary bypass for cooling and rewarming is employed instead of the non-pulsatile bypass.

Recently, some surgeons9,10 have reported on profound hypothermia by using conventional non-pulsatile bypass with acceptable operative results. We carried out studies to determine whether core cooling with pulsatile cardiopulmonary bypass, instead of non-pulsatile bypass cooling in which there has been a high incidence of brain damage11 and metabolic acidosis, can minimize the anaerobic metabolism in the brain tissue.

Profund hypothermia by using cardiopulmonary bypass has great advantages in prolonging the duration of intracardiac procedures with the multiple periods of total circulatory arrest if necessary. In this experiment, the recovery time

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Key Words:
- Hypothermia
- Open-heart surgery in infancy
- Pulsatile cardiopulmonary bypass
- Excess lactate

(Received May 26, 1980; accepted September 25, 1980)
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*Supported by Grant 448273 in Aid for Scientific Research from the Ministry of Education, 1979
Presented at the Fifteenth Annual Meeting of the Society for Cryobiology, August 6–10, 1978, Tokyo, Japan

in the cerebral tissue from anoxic damage due to the first total circulatory arrest was also measured to obtain another arrest period for continued intracardiac repair.

MATERIALS AND METHODS

Adult mongrel dogs weighing 12 kg to 18 kg were cooled down with total cardiopulmonary bypass, and forty minutes of total circulatory arrest was performed, at a brain temperature of 20°C. Cardiac arrest was obtained with aortic cross-clamping. After the first arrest, total bypass was established for 40 minutes, keeping the brain temperature at 20°C. After this intermediate bypass, the second total circulatory arrest was obtained for 20 minutes after which the brain temperature was raised to 35°C with core rewarming, using total cardiopulmonary bypass. The dogs were then sacrificed.

During total bypass, ordinary non-pulsatile blood flow was employed in one group of 10 dogs and pulsatile blood flow, using a pulsatile assist device (Datascope PAD®), Datascope System 42, was employed in another group of 10 dogs.

The venous return cannula was placed in the right ventricle and the right atrium (Fig. 1). Cardiopulmonary bypass was instituted by diverting the venous return into a circuit containing a heat exchanger and a bubble oxygenator (Temptrol, Bentley Laboratories, Inc., Calif). Total bypass was assured by venting the left ventricle and occluding the main pulmonary artery. Arterial blood was returned to the aortic root through the right-angled aortic cannula (No. 49-12305, Sarns International Inc., 3.8 mm in diameter).

The pulsatile assist device was triggered with ECG, when the heart was beating. When the heart was fibrillating or the heart rate decreased, the frequency of pulsatile was controlled manually, depending on the brain temperature (40 times/min between 20°C and 22.5°C, 60 between 22.5°C and 25°C, and 80 between 25°C and 27.5°C). Figures 2 and 3 show the pulsatile waves during the cooling period and intermediate bypass, respectively.

Anesthesia was induced with intravenous sodium pentobarbital, 25 mg per kg, and supplemented with halothane mixed with inspiratory gases or oxygen for the oxygenator, when shivering or spontaneous breathing occurred. After the induction of anesthesia, chlorpromazine 0.5 mg per kg and potassium 0.3 mEq per kg were dripped before the start of core cooling.

The bypass circuit was primed with whole blood obtained on the same day from a single donor dog, and diluted with low molecular weight dextran. During total bypass, the hematocrit was maintained between 20 and 30%, and the systemic flow rate was changed depending on the brain temperature (120 ml/kg/min between 37°C and 30°C, 100 ml/kg/min between 30°C and 27.5°C, 90 ml/kg/min between 27.5°C and 25°C, 80 ml/kg/min between 25°C and 22.5°C, 70 ml/kg/min between 22.5°C and 20°C). Temperature difference between the arterial blood and brain tissue was kept below eight degrees centigrade during both cooling and rewarming.

Carbon dioxide was added to the oxygen delivered to the bubble oxygenator for bypass. Arterial blood gas analysis, and determination of the serum potassium level were frequently performed. The data of arterial blood gas analysis were corrected to the temperature of blood when samples were taken. Carbon dioxide gas for the bubble oxygenator, sodium bicarbonate and potassium were administered to maintain the PaO₂ above 100 mmHg, the PaCO₂ between 30 and 50 mmHg, the pH between 7.3 and 7.5, and

the serum potassium level between 3.5 and 4.5 mEq/L.

Before core cooling, a piece of skull in the parietal region was removed, and a sample of cerebral venous blood was taken from the superior sagittal sinus. The brain temperature was measured by using a needle thermometer probe inserted vertically about 1.0 cm deep into the brain tissue.

Throughout the course of hypothermia, the cerebral excess lactate (ΔXL) (Huckabee)\(^{12}\) was determined by taking samples of the cerebral arterial and venous blood and examining the concentrations of lactate and pyruvate. The formula used in the calculation of the cerebral excess lactate (ΔXL) (millimol per liter) as an index of aerobic or anaerobic metabolism in the cerebral tissue is as follows:

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ΔXL = (Lcv - La) - (Pcv - Pa) \times \frac{(La/Pa)}
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Lcv and Pcv: cerebral venous blood concentrations of lactate and pyruvate
La and Pa: arterial blood concentrations of lactate and pyruvate

RESULTS

Figure 4 shows the changes in the cerebral excess lactate (ΔXL) (millimol per liter) during profound hypothermia in the group assisted with PAD and the group without PAD. During the cooling period, the ΔXL levels were always lower in the pulsatile group than those in the non-pulsatile group. The differences of ΔXL between the two groups were most remarkable and statistically significant during core cooling at 30°C, 27.5°C, 25°C and 20°C (p < 0.01). Throughout the cooling period from 30°C down to 20°C, the mean value of ΔXL (–0.02 ± 0.07 mM/L = Mean ± S.E.M.) in the pulsatile group was significantly lower than that (0.66 ± 0.11) in the non-pulsatile
group (p < 0.01). Thus, it is possible to minimize anaerobic metabolism in the brain during cooling when pulsatile cardiopulmonary bypass is employed for core cooling.

After forty minutes of the first total arrest at a brain temperature of 20°C, total cardiopulmonary bypass was started in order to eliminate the anoxic damage of the brain. During this period, the ΔXL was checked every 10 minutes.

There was no statistically significant difference between the group with PAD and without PAD in the levels of ΔXL during bypass between the first and the second arrest. In both groups, ΔXL was maximum after 20 minutes of bypass and decreased remarkably after 30 minutes of bypass during this intermediate bypass. When the ΔXL levels after 20 and 30 minutes of bypass were compared, no statistically significant difference was apparent. However, in the group with PAD, there was a strong tendency toward decrease of ΔXL levels at 30 minutes after bypass, when compared to the levels at 20 minutes after bypass (p < 0.1).

In the rewarming phase, also, there was no significant difference in the ΔXL level between the two groups.

COMMENT

To determine the time required to eliminate the anaerobic metabolism in the brain by this present method, the duration of the first total circulatory arrest should be within the duration feasible for reverse changes to occur in the brain. There is still controversy over the permissible duration of the circulatory arrest for the brain under deep hypothermia. In the present study, the duration of the first total circulatory arrest was determined by our experimental and clinical results. At the same time, the
studies on gas tension and blood flow in the brain tissue measured by mass spectrometer and radioactive microsphere, respectively, were also referred to in making this determination.

The duration of the bypass time between the first and second total circulatory arrest was determined in preliminary experiments, in which the intermediate bypass was continued until the ΔXL value showed the lowest after the first arrest.

There are a few reports concerning the permissible duration of the second total circulatory arrest. McMurray et al. reported that the second total circulatory arrest time should be shorter than the first one, even when adequate time for recovery is allowed between the two periods of occlusion. Thus, the duration of the second arrest was determined in the present study to be 20 minutes, which is half the time of the first circulatory arrest. If the concentration of the lactate and pyruvate in the cerebral arterial and venous blood is continuously monitored, the permissible duration of the second total arrest can be correctly determined, as the duration of the second arrest would be within the safe period if the maximum level of ΔXL after the second arrest is lower than the maximum level of ΔXL after the first arrest.

Usually partial cardiopulmonary bypass instead of total bypass is employed for core cooling in the clinical cases. At that time, core cooling can be performed with pulsatile flow down to a certain level of low body temperature. However, below a brain temperature of 25°C, the heart rate usually decreases remarkably, and ventricular fibrillation or cardiac arrest readily occurs. For these reasons, therefore, our observations in the present studies are pertinent for clinical cases of profound hypothermia.

There was a statistically significant difference in ΔXL between the two groups among the five checking points during the cooling period, except for the time at 22.5°C. As the mean value of ΔXL at 22.5°C showed a remarkable difference and the mean value of ΔXL of the whole cooling period showed a statistically significant difference between the two groups, the difference of ΔXL value at 22.5°C between two groups would

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probably be statistically significant, with increase in the number of experiments.

One important point is that it takes a few minutes for various metabolites such as lactate and pyruvate to be extruded from the brain tissue into the cerebral veins. Delta excess lactate value showed low levels immediately after the first total circulatory arrest. Namely, there is a time lag between the changes in the level of ΔXL and the actual changes in the metabolism in the brain tissue, so that the actual level of ΔXL after the first circulatory arrest could reach a maximum earlier than 20 minutes. For this reason the recovery time from anoxic damage in the brain may occur before 30 minutes when the total circulatory arrest is obtained at 20°C for 40 minutes.

Metabolism in the brain itself was studied with oxygen consumption21 and mass spectrometry,19 but these methods are unsuitable for examinations related to core cooling for deep hypothermia. Although cerebral excess lactate represents one of the indexes of brain metabolism, this measurement is the only one which can be used to assess the changes of aerobic or anaerobic metabolism in the brain.

During the cooling period, there was a significant difference in ΔXL between the pulsatile and non-pulsatile group, but such differences could not be demonstrated during the intermediate and rewarming periods. The so-called “no-reflow phenomenon”22,23 may be responsible. In our studies, cerebral blood flow was not measured, but Aoyagi et al24 demonstrated that the cerebral blood flow did decrease during the rewarming rather than the cooling period. The same phenomenon probably occurs not only during the rewarming period, but also during intermediate bypass. Thus, even when the pulsatile bypass was employed, this approach cannot overcome decrease of the cerebral blood flow, namely, “no-reflow phenomenon” and differences in ΔXL between the two groups are not as easy to obtain during the intermediate and rewarming periods as during the cooling period.

Since the measurement of cerebral blood flow is important for this kind of experiment, it was attempted, but not successful, as frequent measurements of cerebral blood flow in one experiment using the radioactive microsphere method was impossible. If these measurements were performed only during the cooling period, they might have been obtained. In addition, the correct clearance curve using the hydrogen gas clearance method25 could not be obtained due to the difficulties encountered in mixing the hydrogen gas as a bolus with the circulating blood during bypass.

The role of the pulse pressure in circulatory homeostasis remains unsettled. However, Long and his associates26 noted intravascular aggregation of erythrocytes after prolonged non-pulsatile perfusion resulting in the impairment of the flow in the capillaries and venules. These findings support Wehn’s27 opinion that arterial pulsations contribute to the capillary flow. Especially, under the low body temperature, the poor capillary flow is easily caused by the increased blood viscosity due to the hemoconcentration28,29. It was also found that arterial pulsations exert some measure of control over the exchange rate of the interstitial fluid, lymph and possibly cerebrospinal fluid30. These mechanisms by which arterial pulsations improve tissue viability could be also responsible for the result of Halley, Reemtsma and Creech31 that the oxygen consumption in the brain during non-pulsatile perfusion was decreased despite a normal rate of blood flow and unaltered cerebrovascular resistance. Sanderson, Wright and Sims32 found diffuse nerve cell changes in the brains of dogs perfuse-fixed immediately following two or three hours of non-pulsatile extracorporeal circulation. These experiments suggest that pulsatile flow during cardiopulmonary bypass offers significant advantages in terms of better cellular oxygenation and improved organ function.

Despite the high incidence of brain damage reported by Björk and Hultquist33 some surgeons9,10 advocated the conventional cardiopulmonary bypass during both periods of cooling and rewarming. Cartmill et al9 reported an occasional occurrence of postoperative convulsion, but this cause was not clarified. The present study demonstrated clearly that the anaerobic metabolism in the brain is highly suppressed with a pulsatile cardiopulmonary bypass even when core cooling is employed for profound hypothermia. Thus, the profound hypothermia method with core cooling can be performed more safely if pulsatile cardiopulmonary bypass is employed. Moreover, compared with the combined hypothermia method with surface cooling and core rewarming now being extensively used, this hypothermia method using core cooling and rewarming with a pulsatile flow can shorten the operation time, simplify the hypothermic anesthesia method, and extend the corrective surgery.


MORI A et al
on the more severe infant cardiac patients.

Acknowledgement

We thank Mrs. R. Mitsunami for lactate and pyruvate measurements and M. Ohara, Kyoto University, for advice on the manuscript.

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