The effect of pulsatile perfusion on cerebral blood flow during profound hypothermia with total circulatory arrest

In 39 mongrel dogs, regional cerebral blood flow was measured during pulsatile and nonpulsatile deep hypothermic cardiopulmonary bypass with total circulatory arrest. Total circulatory arrest was performed at 20° C cerebral temperature for 40 minutes in 15 dogs, 60 minutes in 12 dogs, and 80 minutes in 12 dogs. Cerebral blood flow in both groups decreased as cerebral temperature fell and there was no significant difference in cerebral blood flow between the two groups during the cooling period. After circulatory arrest for 40 minutes, as cerebral temperature increased to 35° C, cerebral blood flow in both groups recovered to values as high as the respective initial values, which were measured just after the beginning of cardiopulmonary bypass for cooling ($102.5\% \pm 10.2\%$ in the pulsatile group and $97.2\% \pm 12.6\%$ in the nonpulsatile group). After circulatory arrest for 60 minutes, cerebral blood flow in the pulsatile group increased to $141.8\% \pm 16.1\%$ of its initial value when the cerebral temperature became 35° C, but it remained significantly lower ($64.5\% \pm 9.2\%$) in the nonpulsatile group ($p < 0.01$). After circulatory arrest for 80 minutes, cerebral blood flow in both groups remained lower than the respective initial values. These results suggest that pulsatile perfusion maintains cerebral blood flow even during profound hypothermia and that it may protect the brain from ischemic and hypoxic damage caused by profound hypothermia and total circulatory arrest in cardiac operations. (J THORAC CARDIOVASC SURG 1994;108:119-25)

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Profound hypothermia with total circulatory arrest is a useful technique especially for the repair of congenital cardiac anomalies in children. However, it can be followed by occasional cerebral dysfunction such as seizures, altered consciousness, hypotonia, and paresis. Dysfunction is not always obvious on simple clinical examination but is detected by cerebral injury markers and long-term neuropsychometric follow-up. It may be caused by inadequate perfusion and impaired metabolism of the brain.

Some uncertainty remains regarding the safe limits of circulatory arrest. On the other hand, it has been report-

ed that pulsatile perfusion can maintain the blood flow in many organs during normothermic and hypothermic cardiopulmonary bypass. In the present study, regional blood flow of the cerebral cortex was measured during deep hypothermic cardiopulmonary bypass with total circulatory arrest to assess the effect of pulsatile perfusion on the cerebral blood flow (CBF) in dogs.

Materials and methods

Thirty-nine adult mongrel dogs, weighing between 8 and 13 kg, were divided into two groups: pulsatile group and nonpulsatile group. All dogs were anesthetized with sodium pentobarbital 25 mg/kg intravenously, intubated, and the lungs ventilated with a volume-controlled ventilator. After median sternotomy, cardiopulmonary bypass was established by means of ascending aortic cannulation and venous drainage from the right atrium (Fig. 1). Total bypass was assured by venting the left ventricle and occluding the main pulmonary artery. A pulsatile assist device (driven by System 42, Datascope Corp., Paramus, N.J.) was interposed in the arterial line for the pulsatile perfusion, and pulse pressure of more than 25 mm Hg was maintained in the pulsatile group during cardiopulmonary bypass. Each dog was

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Fig. 1. Extracorporeal circulation circuit. Ao, Ascending aorta; PA, pulmonary artery; RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle; PAD, pulsatile assist device.

cooled to a 20° C cerebral temperature by cardiopulmonary bypass, and then total circulatory arrest was performed for 40, 60, or 80 minutes in each group. After the total circulatory arrest, cardiopulmonary bypass was started again and the dog was rewarmed to 35° C cerebral temperature. During cardiopulmonary bypass, mixed gas of oxygen and carbon dioxide was blown into the membrane oxygenator (Capiiox II, Terumo Corp., Tokyo, Japan). Blood samples were obtained from the catheter placed in the descending aorta, and blood gas analysis was done. Readings of arterial gas analysis were corrected for blood temperature. Arterial oxygen tension was maintained higher than 200 mm Hg, and arterial carbon dioxide tension was maintained between 25 and 35 mm Hg during cardiopulmonary bypass. The cerebral temperature was measured with the use of a needle-shaped temperature probe inserted about 1 cm into the temporal lobe contralateral to the lobe where the cerebral tissue blood flow was measured. Blood temperature was measured with a thermometer that was built into the cardiopulmonary bypass circuit.

Perfusion flow rate was changed according to the cerebral temperature as follows: 35° to 30° C, 100 ml/kg per minute; 30° to 25° C, 80 ml/kg per minute; and 25° to 20° C, 60 ml/kg per minute. The pulse rate made by the pulsatile assist device was also changed as follows: 35° to 27.5° C, 100 beats/min; 27.5° to 25° C, 80 beats/min; 25° to 22.5° C, 60 beats/min; and 22.5° to 20° C, 40 beats/min.

During cardiopulmonary bypass, regional CBF in the cortex of the parietal lobe was measured at 35°, 30°, 25°, and 20° C cerebral temperature by a hydrogen gas clearance method. An amplifier (MHG-D1, Unique Medical Co. Ltd., Tokyo, Japan) and a recorder (Servocorder, SR-6312, Graphtec Co. Ltd., Tokyo, Japan) were used for measurements. The electrodes (UHE-100, Unique) used to measure hydrogen concentration were inserted into the cerebral cortex 2 to 3 mm in depth through the dura mater after craniotomy (2 × 2 cm) was done in the left temporal bone. Hydrogen gas was delivered into the oxygenator. CBF was calculated from the slope of the hydrogen concentration curves plotted on semilogarithmic paper according to the

formula $F/W = 69.3/T^{1/2}$, where F/W is blood flow (ml/min/100 gm of tissue) and $T^{1/2}$ is the half-time of hydrogen gas desaturation.

All values were expressed as mean values plus or minus the standard error. The statistical analyses were done by means of Student's *t* test and the values were considered significant if the probability value (*p*) was less than 0.05.

All dogs received humane care in accordance with the "Principles of Laboratory Animal Care" (National Society for Medical Research), the "Guide for the Care and Use of Laboratory Animals" (NIH Publication No. 86-23, revised 1985, National Institutes of Health), and the "Guide for the Use of Laboratory Animals" (Institute for Experimental Animals, Shiga University of Medical Science).

Results

The cardiopulmonary bypass time was 170.7 ± 7.2 minutes in the pulsatile group and 177.0 ± 13.4 minutes in the nonpulsatile group, and no significant difference was detected between the two groups.

Regional CBF during cardiopulmonary bypass is shown in Figs. 2 through 7. CBF at the beginning of cardiopulmonary bypass for cooling was 42.4 ± 2.8 ml/min/100 gm in the pulsatile group and 40.2 ± 2.8 ml/min/100 gm in the nonpulsatile group, and no significant difference was detected between the two groups. CBF decreased gradually during the course of the cooling period in both the pulsatile and nonpulsatile groups, again with no significant difference between the two groups.

In the 40-minute arrest series (Figs. 2 and 3), CBF in the pulsatile group at 20° C, which was measured 5 minutes after the initiation of cardiopulmonary bypass for rewarming, was significantly higher than that in the nonpulsatile group (52.1 ± 7.0 ml/min/100 gm in the pulsatile group and 29.2 ± 5.4 ml/min/100 gm in the nonpulsatile group). Although the CBF in the pulsatile group tended to be higher than that in the nonpulsatile group during the rewarming period, no significant difference was observed between the two groups except at 20° C. When the cerebral temperature was rewarmed to 35° C, CBF in both groups recovered to values as high as the respective values at the beginning of cardiopulmonary bypass (42.5 ± 6.1 ml/min/100 gm in the pulsatile group and 39.6 ± 5.1 ml/min/100 gm in the nonpulsatile group).

In the 60-minute arrest series (Figs. 4 and 5), the CBF in the pulsatile group increased to $141.8\% \pm 16.1\%$ of the initial value as the cerebral temperature rose to 35° C during the rewarming period, but CBF in the nonpulsatile group remained lower ($64.5\% \pm 9.2\%$). The CBF in the pulsatile group was significantly higher than that in the nonpulsatile group at 30° and 35° C during the rewarming period.

Fig. 2. CBF in 40-minute arrest group. SE, Standard error.

Fig. 3. Percent CBF in 40-minute arrest group. SE, Standard error.

In the 80-minute arrest series (Figs. 6 and 7), the CBF in both groups remained significantly lower than the respective initial values when the cerebral temperature increased to 35° C (67.3% ± 15.2% in the

pulsatile group and 46.3% ± 8.9% in the nonpulsatile group). No significant difference was observed between the two groups during the rewarming period.

Fig. 4. CBF in 60-minute arrest group. SE, Standard error.

Fig. 5. Percent CBF in 60-minute arrest group. SE, Standard error.

Discussion

It has been reported that pulsatile perfusion during cardiopulmonary bypass affords the following benefits: renal function is well maintained during the operation,¹⁻³ blood flow in many organs is well preserved,⁴ microcircu-

lation is preserved,⁵ aerobic metabolism and oxygen consumption are adequately maintained,⁶ low vascular resistance and afterload reduction positively affect post-operative heart function,⁷ the renin-angiotensin system is inhibited,⁸ and glucose and lipid metabolism is main-

Fig. 6. CBF in 80-minute arrest group. *SE*, Standard error.

Fig. 7. Percent CBF in 80-minute arrest group. *SE*, Standard error.

tained appropriately.⁹ It has also been reported that even during hypothermia, temperature differences between various organs are minimized¹⁰ and the CBF and aerobic metabolism are better maintained by pulsatile perfusion

than nonpulsatile perfusion.¹¹ Therefore pulsatile perfusion was expected to have a significant effect, especially in patients whose preoperative condition was poor and who would require prolonged cardiopulmonary bypass

with hypothermia. On the basis of these suppositions, we applied pulsatile perfusion to a method of profound hypothermia with total circulatory arrest combined with cardiopulmonary bypass. We have previously reported experimental results on the effect of pulsatile perfusion on abdominal organs in the liver, pancreas, and kidney during profound hypothermia and total circulatory arrest.⁴

Serious postoperative complications after profound hypothermia and total circulatory arrest include neurologic abnormalities. Except for the obvious embolism, longer cerebral ischemia, decreased CBF, and microcirculation disorders have been thought to be the causes of postoperative neurologic abnormalities.¹²⁻¹³ On the other hand, it has been reported that pulsatile perfusion during hypothermia resulted in fewer changes to the cerebral microvessels,¹⁴ less sludging of the blood,¹⁴ and fewer ischemic changes to the neurons.¹⁵ Also, abnormal electroencephalograms were clinically less frequent after profound hypothermia and circulatory arrest, and recovery of consciousness after the operation occurred faster, so that cerebral function was reestablished earlier after pulsatile perfusion than after nonpulsatile perfusion.¹⁶⁻¹⁷ In this study, the effect of pulsatile perfusion on CBF during profound hypothermia with total circulatory arrest was discussed. Blood flow in the cerebral cortex was measured by the hydrogen gas clearance method described by Aukland, Bower, and Berliner¹⁸ in 1964.

In the first experiment in which circulatory arrest was administered for 40 minutes, CBF at 20° C during the rewarming period was higher than that measured just before circulatory arrest in both groups (the pulsatile group and the nonpulsatile group). Even during profound hypothermia of 20° C, cerebral metabolism might continue to function, and the metabolites would accumulate in the tissue. Therefore it was suggested that the pH of cerebral tissue might decrease, resulting in the dilation of cerebral resistant vessels and an increase in CBF. In this study, the CBF in the pulsatile group was higher than that in the nonpulsatile group; thus it was expected that accumulated metabolites would be washed out more rapidly in the pulsatile group. In fact, Watanabe and associates¹⁹ reported that pulsatile perfusion was more effective than nonpulsatile perfusion in bringing about a recovery in pH and carbon dioxide tension in the cerebral tissue during the rewarming period.

In the 60-minute circulatory arrest experiment, CBF in the pulsatile group increased to $141.8\% \pm 16.1\%$ of the initial value when the cerebral temperature rose to 35° C during the rewarming period, but CBF in the nonpulsatile group remained significantly lower ($64.5\% \pm 15.2\%$, $p < 0.01$). In the 80-minute circulatory arrest experiment, CBF in both groups remained lower than the

respective initial values ($67.3\% \pm 15.2\%$ and $46.3\% \pm 8.9\%$ at 35° C cerebral temperature) and did not recover during the rewarming period. It is thought that the CBF could not be improved and remained lower during the rewarming period because of the so-called "no-reflow phenomenon." With respect to the CBF, the maximum time of cerebral ischemia at 20° C was thought to be about 40 to 60 minutes, as many other investigators have reported. On the basis of the results of this study, it is suggested that pulsatile perfusion could allow for a longer period of cerebral circulatory arrest than nonpulsatile perfusion.

The results of this study suggest that pulsatile perfusion may have many advantages over nonpulsatile perfusion under conditions of profound hypothermia and particularly during profound hypothermia with total circulatory arrest. Blood flow in the cerebral cortex can be improved and a longer period of circulatory arrest may be possible with the use of pulsatile perfusion. Therefore it is expected that the clinical application of pulsatile perfusion to profound hypothermia with total circulatory arrest may prevent deterioration in the function of the brain and other organs caused by decreased blood flow in tissues.

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