EXPERIMENTAL AND CLINICAL OBSERVATIONS ON THE USE OF HYPOTHERMIA TO PREVENT ISCHEMIC DAMAGE TO THE CENTRAL NERVOUS SYSTEM*

Robert G. Pontius, M.D., and Michael E. De Bakey, M.D.**

The tissues of the central nervous system are particularly vulnerable to ischemic damage from even brief periods of circulatory arrest. This constitutes a serious hazard in the performance of certain cardiovascular procedures such as resection of aortic aneurysm, in which it may be necessary to interrupt aortic circulation for periods up to one hour[4]. Since it has been well established that hypothermia reduces total body metabolism and oxygen requirements of tissues, it is reasonable to assume that the central nervous system is similarly affected and that this might provide a useful measure in minimizing the ischemic dangers associated with these operative procedures[2, 3]. Accordingly, studies have been directed toward determining the protective value of hypothermia against such ischemic damage to the central nervous system during periods of temporary aortic occlusion.

Experiments along these lines have been done by a number of investigators as well as by us[1, 7,-12]. Thus, in a control group of 50 dogs occlusion of the aorta just distal to the left subclavian artery for a period of one hour was associated with an immediate mortality of 32 per cent and a

*Supported in part by grants from the Houston Heart Association and the Cora and Webb Mading Fund for Surgical Research.

**From the Department of Surgery, Baylor University College of Medicine, and the Surgical Services of the Jefferson Davis, Veterans Administration, and Methodist Hospitals, Houston, Texas.

paraplegia rate in the surviving animals of 65 per cent. The same procedure in a comparable group of 47 hypothermic dogs (body temperature was reduced to between 75 and 80° F.) was associated with an immediate mortality of 25 per cent and with a paraplegia rate of zero in the surviving animals. (Fig. 1) On the basis of these experiments as well as similar observations reported by other workers, the conclusion has been drawn that hypothermia has a definite protective influence against ischemic damage to the spinal cord following high aortic occlusion.

While the exact mechanism of protection afforded by hypothermia is not entirely clear, gross and histologic studies of the damaged spinal cord provide some clues to the problem. Gross examination of the spinal cords of the paraplegic animals showed bilateral symmetrical malacia of the grey matter of the lumbar, sacral, and coccygeal segments. Serial sections showed the lesions to begin consistently between T_{12} and L_2 and continue distally. On microscopic examination pronounced changes were present in the grey matter, but the white matter was spared. As the specimens were obtained 12 days after injury evidence of repair by microglial phagocytes or gitter cells with foamy cytoplasm and proliferation of new capillaries through the destroyed area was present (Figs. 2, 3, 4). These changes are quite similar to those observed in the brain following anoxemic damage to this organ. They do not suggest thrombosis or infarction as the vessel lumens were patent. The animals protected by

hypothermia failed to show these changes.

Experiments along similar lines directed toward determining the protective effects of hypothermia against ischemic damage to the brain proved much more difficult, owing to the fact that in the dog extensive collateral circulation exists in the head and neck. Thus, occlusion of both carotid and vertebral arteries bilaterally produced no apparent disturbances. A preparation was finally developed, however, that resulted in a significant incidence of brain damage. This consisted in placing a silver clip on the basilar artery through the foramen magnum, applying occluding clamps to both carotid and vertebral arteries bilaterally and placing a tourniquet around the neck to produce compression of the muscular collateral vessels. In the control group of 9 dogs in which this was done for a period of 30 minutes, 6 (67 per cent) showed serious brain damage as manifested by convulsions, coma, and death. Significantly, none of the 9 hypothermic dogs treated in like fashion developed any neurologic disturbances. These observations, therefore, suggest that hypothermia is equally effective in preventing ischemic damage to the brain as to the spinal cord following temporary arrest of the circulation to these highly vulnerable tissues.

These experimental observations on the protective value of hypothermia in preventing ischemic damage to the central nervous system are supported by our clinical experience with its use in the excisional therapy of aortic aneurysm. In such cases in which the lesion is located in the

thoracic aorta above the level of the seventh dorsal vertebra the procedure of resection and graft replacement is associated with the jeopardous effects of ischemic injury to the tissues of the central nervous system during the period of temporary interruption of aortic circulation. Thus, among the five cases of aneurysm of the aorta in our series, located at this high level and treated by resection without hypothermia, spinal cord damage occurred in four patients (Fig. 5). Fortunately these changes were mild and transient in three, but probably contributed to the death of the fourth patient.

On the other hand, none of the 14 cases with comparable lesions similarly treated but in which hypothermia was employed showed any manifestations of spinal cord damage. Both in this as well as the former group the period of aortic occlusion averaged about one hour. In the hypothermic group body temperature was reduced to about 85° F. (Figs. 6, 7).

SUMMARY

1. In a control group of 50 dogs in which the thoracic aorta was occluded just distal to the left subclavian artery for a period of one hour the immediate mortality was 32 per cent and the incidence of ischemic damage to the spinal cord as manifested by paraplegia in the surviving animals was 55 per cent. In a comparably treated group of 47 dogs in which hypothermia was used there was an immediate mortality of 25 per cent, but none developed paraplegia.

2. In a control series of 9 dogs in which the circulation to the brain was arrested for a period of 30 minutes evidence of ischemic damage to the brain occurred in 6 (67 per cent), but none of the 9 similarly treated group in which hypothermia was employed showed such manifestations.

3. Four of five patients with aneurysms of the thoracic aorta in whom the aorta was occluded for a period of about one hour developed evidence of spinal cord damage following resection. None of 14 similar cases in which hypothermia was employed developed any evidence of spinal cord damage.

4. On the basis of these experimental and clinical observations it would appear that hypothermia increases the tolerance of the tissues of the central nervous system to periods of temporary ischemia.

LEGENDS

Figure 1: Graph showing mortality for occlusion of descending thoracic aorta for one hour.

Figure 2: Microscopic section of normal spinal cord, L_2 level, of dog.

Figure 3: Microscopic section of spinal cord following aortic occlusion without hypothermia.

Figure 4: Microscopic section of spinal cord following aortic occlusion with hypothermia.

Figure 5: Chart of clinical cases without hypothermia.

Figure 6 and 7: Chart of clinical cases with hypothermia.

BIBLIOGRAPHY

1. Beattie, E. J., Jr., Adovasio, D., Keshishian, J. M., and Blades B.: Refrigeration in Experimental Surgery of the Aorta, Surg., Gynec. & Obst. 96: 711-713 (June) 1953.
2. Bigelow, W. G., Callaghan, J. C., and Hoppe, J. A.: General Hypothermia for Experimental Intracardiac Surgery, Ann. Surg. 132: 531, 1950.
3. Bigelow, W. G., Lindsay, W. K., Harrison, R. C., Gordon, R. A., and Greenwood, W. F.: Oxygen Transport and Utilization in Dogs at Low Body Temperatures, Am. J. Physiol. 160: 125, 1950.
4. Carrel, A.: Report on the Experimental Surgery of the Thoracic Aorta and Heart, Ann. Surg. 52: 83, 1910.
5. De Bakey, M. E., and Cooley, D. A.: Excisional Therapy of Aortic Aneurysms, Am. Surg. 19: 603 (July) 1953.
6. Gross, R. E.: Coarctation of the Aorta, Circulation 7: 757 (May) 1953.
7. Gross, R. E., and Hufnagel, C. A.: Coarctation of the Aorta: Experimental Studies Regarding Its Surgical Correction, New Eng. J. Med. 233: 287, 1945.
8. Parkins, W. M., Jensen, J. M., and Vars, H. M.: Brain Cooling in the Prevention of Brain Damage During Periods of Circulatory Occlusion in Dogs, Ann. Surg. 140: 284, 1954.

9. Parkins, W. M., Ben, M., and Vars, H. M.: Tolerance of Temporary Occlusion of the Thoracic Aorta in Normothermic and Hypothermic Dogs, Surgery 38: 38, 1955.

10. Pontius, R. G., Bloodwell, R. D., Cooley, D. A., and De Bakey, M. E.: The Use of Hypothermia in the Prevention of Brain Damage Following Temporary Arrest of the Cerebral Circulation: Experimental Observations. Surgical Forum, Clinical Congress of the American College of Surgeons, 1954. pp. 224-228

11. Pontius, R. G., Brockman, H. L., Hardy, E. G., Cooley, D. A., and De Bakey, M. E.: The Use of Hypothermia in the Prevention of Paraplegia Following Temporary Aortic Occlusion: Experimental Observations, Surgery 36: 33, 1954.

12. Watkins, E., Jr.: Circulatory Changes Produced by Clamping of the Thoracic Aorta, Surgery 22: 530, 1947.