TOLERANCE OF CIRCULATORY ARREST IN DEEP HYPOTHERMIA BY EXTRACORPOREAL COOLING

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The advantages of moderate hypothermia in the range of 26°–30°C. have been well established for certain operations on the brain and cases of brain injury. During the past few years some investigators have become interested in the development of a method that would satisfactorily achieve deeper levels of hypothermia of the brain, in order that neurosurgeons might be allowed to work on a brain with greater "fall-away," less bleeding, and with greater tolerance to temporary occlusion of the large vessels of the neck. Parkins, Lougheed, and Woodhall have done animal experimentation with selective cooling of the brain by perfusing the carotid arteries with cold blood. This method was used in this laboratory on 30 dogs, and it was found that cooling of the brain to 10°–15°C. was entirely compatible with survival in many cases. However, in too many cases there was drifting of the body temperature below 25°C. with ventricular fibrillation resulting. Also there were other contraindications to application of this procedure to patients, in that it would require cannulation of the carotid arteries and the continuous circulation of blood to the brain during the definitive operative procedure. Some of the latest reports in the clinical field include that of Drew of England in which two pumps were used and the patient’s lungs acted as an oxygenator. The same technic was employed by Björk of Sweden. In this country, the leading reports are by Sealy et al. In France, work has been done by Dubost. He, like most authors, did his work in the field of cardiac surgery. In the field of neurosurgery, reports so far are few, and we can cite only the work of Woodhall et al., and the report of Uihlein et al. More clinical results are necessary in order to make a correct evaluation of the method. Thus it was felt that total cooling of the body to a very low temperature by extracorporeal circulation should be investigated. This procedure, as described by Gollan and Brown et al., potentially affords an ideal situation for the neurosurgeon. With the body cooled to levels producing cardiac arrest, the extracorporeal circulation could be stopped for a duration more than adequate to allow definitive handling of the cerebral lesion without significant hemorrhage. It would appear that if this method could be developed into a reliable procedure, without risk of additional morbidity or mortality, it would offer significant advantages to the surgical therapy of cerebral vascular lesions and certain neoplasms.

METHOD

Forty-five apparently healthy mongrel dogs weighing 10 to 20 kg. were used. Intravenous thiopental sodium anesthesia was used in 37 dogs. In 36 of these dogs, thiopental sodium was used for induction and maintenance of anesthesia until cooling had progressed to the level (26°–28°C.) at which it was no longer needed. In one dog thiopental sodium was used for induction only, after which paralysis was maintained by succinylcholine. Of the remaining 8 dogs in this series, 7 were anesthetized with intravenous pentobarbital sodium, 25 mg./kg., and 1 dog was induced with ether and maintained on N₂O, 100 per cent O₂, and succinylcholine. Phenergan, 50 mg., was given intramuscularly to 12 dogs with thiopental sodium anesthesia. The other dogs received no premedication. Endotracheal intubation was performed on all dogs. Twenty-three dogs were respirated mechanically until 25°C., at which...
point the respirator was discontinued and then started again during the warming phase at the same temperature. Seventeen dogs were respirationally ventilated mechanically throughout the entire procedure, including the period of circulatory arrest. Three dogs were ventilated manually with 100 per cent O\textsubscript{2}, while 2 dogs were allowed to breathe spontaneously. Heparin sodium 2 mg./kg. was administered prior to cannulation of vessels. Catheters for outflow to the oxygenator were introduced into the femoral and external jugular veins and passed into the inferior and superior venae cavae, respectively. A catheter for arterial inflow from the oxygenator was introduced 2-4 cm. into the femoral artery. The dissections and cannulations were simple and required, at the most, 30-45 min.

The extracorporeal circuit consisted of a modified Dewall helix reservoir bubble oxygenator and a dual Sigmanator pump, with a heat exchanger interposed in the arterial line. In the first 14 dogs of the series, a metal coil immersed in ice water was used for heat exchange, while in the remainder of the dogs a Harrison-Brown heat exchanger \textsuperscript{2} was used. To prime the extracorporeal circuit, 1500 cc. of fresh donor blood was required. This was obtained by exsanguination of donor dogs which had received heparin sodium 1 mg./kg. An additional dose of heparin sodium, 20 mg./500 cc., was added to the donor blood. This blood was oxygenated prior to the perfusion.

A partial cardiopulmonary by-pass thus was achieved following connection of the extracorporeal circuit to the catheters in the dog. Venous outflow to the oxygenator was achieved by direct suction on the venous catheters. Oxygenation was effected by a flow of 1-2 liters of 100 per cent O\textsubscript{2}, the volume depending upon the rate of flow of blood required. The rate of arterial blood flowing into the dog was maintained as close as possible to 40 cc./kg. above an esophageal temperature of 32°C, and 30 cc./kg. below 32°C.

Prior to cooling, all dogs except 4 received quinidine gluconate, 30 mg./kg., diluted in 50 cc. normal saline, by intravenous infusion, which was given in an average of 25 min. The infusion was completed, on an average, 32 min. prior to cooling. In 3 dogs the same dose of quinidine gluconate was added to the donor blood, so that they received it by arterial infusion as cooling progressed. One dog received no quinidine.

The rate of cooling was somewhat more rapid in the first 14 dogs in which the metal coil heat exchanger was used. In these dogs perfusion was started approximately 15 min. prior to immersion of the coil in ice water. During this time the esophageal temperature dropped to an average level of 32°C, since the blood was cooled by room air during its passage through the extracorporeal circuit. Following this initial period of circulation, the coil was then placed in the ice water and rapid cooling to low temperatures resulted. In the remainder of the procedures in which the Harrison-Brown heat exchanger was used, the esophageal temperature was lowered more gradually by a stepwise reduction of temperature of the water entering the heat exchanger. In these cases ice water was not circulated through the heat exchanger until esophageal temperature had reached 25°C.

The dogs were cooled to an average esophageal temperature of 5.5°C. The extracorporeal circulation was then discontinued for 45 min. in 22 dogs, periods between 10 and 35 min. in 15 dogs, 60 min. in 1 dog, and 120 min. in 5 dogs. In the 5 dogs with circulatory arrest for 120 min., cooling of the surface in addition to cooling of the blood stream was used.

Rewarming to normothermic levels was accomplished by resuming the extracorporeal circulation and gradually elevating the temperature of water surrounding the metal coil or circulating through the heat exchanger. The rates of flow again were maintained at 30 cc./kg. below 25°C, and 40 cc./kg. above 25°C. The extracorporeal circulation was discontinued at an average esophageal temperature of 36°C., a transfusion of whole blood was given, and the catheters were removed. Propramine sulfate was administered by intravenous injection in a ratio of 1.5 mg.:1 mg. of heparin sodium. The wounds then were closed and the dogs were allowed to survive.

A Sanborn model 150 recording system was used to monitor simultaneously electrocardiogram, electroencephalogram, arterial and venous blood pressures, and esophageal, cerebral and rectal temperatures. Statham pressure transducers P 23AA and P 23BB were connected to catheters in the femoral vein and artery for the blood-pressure recordings. A multiple thermocouple apparatus was used for recording of temperature and was calibrated carefully before the procedures with standard mercury thermometers. Temperature of the brain was recorded from a thermocouple introduced into the cerebral cortex through a small drill hole. Hematocrits were run frequently during all procedures, arterial blood pHs were determined frequently in 22 dogs, venous oxygen saturations were done in 2 dogs, and venous and arterial blood CO\textsubscript{2} determinations were done in 2 dogs.

RESULTS

The survival rate for the series, with varying periods of circulatory arrest, is indicated in Table 1. Four dogs that underwent large craniectomies were sacrificed acutely and thus are not included in this table. Duration