Physiologic Studies Following Closed-Chest Technique of Profound Hypothermia in Neurosurgery

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Postoperative physiologic studies were carried out in 6 patients after repair of intracranial aneurysm with the aid of profound hypothermia induced by a closed-chest perfusion technique. Hemodynamic studies indicated some impairment in myocardial function in one patient and hypovolemia in one patient; in 3 patients results were normal. Acid-base determinations showed a tendency toward metabolic acidosis on the evening of operation. This tendency probably was secondary to the comparatively low flow rates utilized for perfusion. Buffer base was lowest in the 2 patients who were exposed to prolonged periods of low flows at 15° C. Postoperative oxygen saturations of patients breathing room air were somewhat below normal, but clinically they were not significant. Comparison of these data with data previously obtained on patients cooled by an open-chest perfusion technique indicates little difference between the two techniques in relation to postoperative hemodynamic, metabolic and pulmonary functions.

PROFOUND hypothermia and total circulatory arrest have been utilized at the Mayo Clinic in the surgical repair of intracranial aneurysms since March 1960. Initially repair was accomplished with an open-chest technique similar to that described by Drew for cardiac surgery. A closed-chest perfusion technique has been utilized for the past 18 months and is presently the method of choice at this institution. This is a report on postoperative physiologic studies performed on several patients in the closed-chest group and a comparison with similar observations made in the open-chest group.

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Procedure and Material

Six patients with intracranial aneurysms in whom surgical repair was accomplished with the aid of profound hypothermia produced by the closed-chest technique were studied. All of the patients were neurologically intact prior to operation, although 4 patients had experienced one or more episodes of bleeding from the aneurysm. Anesthesia followed premedication with 0.4 mg. of atropine and was induced with cyclopropane or halothane. After intubation with the aid of 60 mg. of succinylcholine, anesthesia was maintained with 0.5 to 1.0 per cent of halothane and 50 per cent nitrous oxide in oxygen (total flow rate, 5 liters per minute). The lungs of all patients were hyperventilated utilizing a Bird ventilator with positive-negative pressure phasing. During craniotomy and exposure of the femoral vessels the patients were cooled to 30° to 32° C. on Therm-O-Rite blankets. During this time 80 to 120 mg. of gallamine triethiodide (Flaxedil) was used to prevent shivering.

After heparinization (90 mg./m.^{2}), both common femoral veins and one femoral artery were cannulated and bypass through a small Mayo-Gibbon pump oxygenator was instituted. The perfusate consisted of 1,500 ml. of ACD blood, 1,500 ml. of 5 per cent dextrose in water, 240 ml. of serum albumin, 45 mg. of heparin, and 1,500 mg. of calcium chloride (10 per cent). The blood was cooled with a modified Brown-Emmons heat exchanger. During cooling and rewarming, esophageal and nasopharyngeal temperatures were used as indexes of heart and brain temperatures, respectively. Flow rates ranged from 1.1 to 1.7 liters per minute per square meter of body surface and were augmented by the cardiac output until ventricular fibrillation or

TABLE 1. Perfusion Data: Profound Hypothermia (Closed Chest)*

Case	Age (years)	Cooling Time (minutes)	Low Flows (0.6–1.0 l./min./m.²) × (minutes)	Arrest		Rewarming Time (minutes)	Flow Rate (l./min./m.²)	Total Transfusion (liters)
				Time (minutes)	Temperature (degrees C.)			
1	56	43	0	12	16	53	1.3	3
2	58	38	0	13	15	30	1.4	5
3	22	20	27	0	16†	42	1.35	3.5
4	59	28	0	7	14	20	1.2	7
5	52	32	55	0	15†	43	1.7	6
6	46	46	0	7	19	51	1.1	3.5

* All patients survived.
† Low flows established at this temperature.

ineffective cardiac function was produced by the cooling process (24° to 27° C., esophageal). At this point ventilation was terminated. During cooling, 7 per cent carbon dioxide was introduced into both the oxygenator and the lungs for the purpose of producing cerebral vasodilatation.[6] When the nasopharyngeal temperature reached 15° C. either low flows (0.6 to 1.0 liter/minute/m.²) or total circulatory arrest was established by stopping the pumps. After repair of the aneurysm, rewarming was accomplished with flow rates of 1.1 to 1.7 liters per minute per square meter of body surface. At an esophageal temperature of 26° to 28° C. the heart was easily defibrillated externally with an AC defibrillator and ventilation was resumed. Extracorporeal circulation was terminated and hexadimethrine bromide (Polybrene) (135 mg./m.²) was administered at temperatures of 32° to 34° C. Further rewarming to 37° C. was accomplished with Therm-O-Rite blankets during closure of the craniotomy. The anesthetic time varied from 5 to 8 hours. Postoperative care was considered to be routine in all but case 5; in this patient tracheostomy was performed on the second postoperative day.

Measurements were carried out in the postoperative period at normal body temperature on the evening of operation (day 1), as well as on the second and third postoperative days

TABLE 2. Hemodynamics after Profound Hypothermia (Closed Chest)

Case	Day	Cardiac Index (l./min./m.²)	Heart Rate (beats/minute)	Stroke Index (ml./m.²)	Pressure (mm. Hg)		Temperature (degrees C.)
					Arterial	Venous	
1	1	5.4	110	49	155/73	6	37
	2	4.0	93	43	122/63	2	38
	3	4.5	80	56	139/64	5	38
2	1	3.2	63	51	205/92	12	37
	2	2.5	48	53	146/58	5	38
	3	—	48	—	144/61	5	38
3	1	4.2	90	47	138/70	—	36
	2	4.5	110	40	173/82	—	38
	3	3.9	87	45	138/66	—	39
4	1	3.0	120	25	140/90	10	36
	2	2.7	90	30	102/64	11	37
5	1	2.8	133	21	161/81	0	36
	2	2.4	160	14	139/82	−1	38

(day 2 and day 3). By means of a cannula previously placed in a radial artery and a catheter passed to the approximate level of the superior vena cava by way of an antecubital vein, values for cardiac output (dye-dilution technique), pressures (strain-gauge), blood gas contents (Van Slyke and Neill), *p*H (37° C.), arterial P_{CO_2} and buffer base (Singer and Hastings), oxygen saturation, and hemoglobin were obtained as previously described.[5, 7]

Results

All patients studied survived the procedure, and except for one patient (case 5) in whom postoperative aphasia developed, recovery was complete. Perfusion data (table 1) include flow rates provided by the pump-oxygenator during cooling and rewarming (1.1 to 1.7 liters/minute/m.^{2}), total perfusion times (48 to 130 minutes), and, in four patients, total circulatory arrest times (7 to 13 minutes). In the other two patients circulatory arrest was not utilized but prolonged periods of low flows (0.6 to 1.0 liter/minute/m.^{2}) were instituted after the desired temperature was reached. At the time of circulatory arrest or low flow, nasopharyngeal temperature ranged from 14° to 19° C. The volume of ACD blood transfused ranged from 3 to 7 liters.

Hemodynamic observations were made in cases 1 to 5 inclusive and are shown in table 2. Cardiac index was within normal range (2.8 to 5.4 liters/minute/m.^{2}) on the evening of operation (day 1), and, with the exception of case 2, was associated with an increase in heart rate. In cases 4 and 5 stroke index was below normal and was associated with the greatest increase in heart rate. Except in case 3, cardiac index decreased on day 2, and in all but case 5 the decrease was associated more with a fall in heart rate than with stroke index. The two patients studied on day 3 demonstrated normal cardiac and stroke indexes and heart rate. Venous pressure was not observed in case 3, was normal in cases 1 and 2, high in case 4, and low in case 5.

The variations from normal seen in the first three cases are not of a significant degree. In case 5 the patient was intentionally undertransfused during operation in the hope of minimizing venous oozing; this procedure accounts for the combination of low venous pressure, low stroke index, and elevated heart rate. The craniotomy wound was explored the eve-

TABLE 3. Acid-Base Balance and Oxygen Saturation after Profound Hypothermia (Closed Chest)

Case	Day	*p*H	P_{aco_2} mm. Hg	BB+ (mEq./l.)	S_{ao_2} (%)	Hemoglobin (g./100 ml.)
1	1	7.39	41	48	85	14
	2	7.36	42	46	93	13
	3	7.39	37	46	93	12
2	1	7.33	45	46	94*	16
	2	7.44	35	49	91	16
	3	7.43	38	50	88	15
3	1	7.32	43	42	95	13
	2	7.44	33	49	97	12
	3	7.48	33	49	97	10
4	1	7.32	38	42	97	13
	2	7.47	39	51	93	13
5	1	7.21	46	40	94	13
	2	7.42	37	46	96	12
6	1	7.31	48	46	95	16
	2	7.49	35	53	95	16

* In oxygen tent.

ning of operation and an intracranial hematoma was evacuated. Again he was undertransfused intentionally and the studies on day 2 again supported the diagnosis of hypovolemia.

The observations in case 4 are more difficult to interpret. In this case the combination of high venous pressure, low stroke index and elevated heart rate as seen on day 1 suggests myocardial impairment rather than hypovolemia. Nevertheless, a transfusion of 2,000 ml. of blood was given to this patient between the studies on day 1 and day 2. The transfusion did not result in further elevation of the venous pressure, and both stroke index and heart rate showed some improvement. It is possible that a combination of impaired myocardial function and hypovolemia existed on day 1, and with sufficient improvement in cardiac function by day 2 the transfused blood was well tolerated by the patient. It is of interest that this patient had the shortest total perfusion time (48 minutes) of those studied.

Values for arterial *p*H, P_{CO_2}, buffer base, oxygen saturations, and hemoglobin are listed in table 3. On day 1 the *p*H was below normal in all but case 1. This was due primarily to a reduction in buffer base in cases 3, 4 and 5, although mild retention of carbon dioxide was present in case 5 as well as in cases 2 and 6. By day 2 the values for *p*H, P_{CO_2}, and buffer base had returned toward normal in all patients. In general, no further changes were observed on day 3. While the patients breathed room air, arterial oxygen saturations were slightly below normal and isolated low values were seen in cases 1 and 2.

The consistent decrease in *p*H seen on day 1 and the associated low or low normal buffer base (except case 1) is not surprising in view of the relatively low flow rates provided by the pump-oxygenator during the period of ineffective cardiac action. The lowest observed *p*H (7.21) and buffer base (40 mEq./liter) were in case 5. This patient received the highest flow rates during cooling and rewarming (1.7 liters/minute/m.^{2}) but also had a prolonged period (55 minutes) of low flow at 15° C. and was the same patient who was maintained in a hypovolemic state. Another patient (case 3) also had a prolonged period (27 minutes) of low flow at 16° C. and likewise showed a low buffer base on day 1 (42 mEq./liter). The only other significantly low buffer base was observed in case 4 (42 mEq./liter); this patient was thought to have some impairment of cardiac function on day 1. The return to a normal *p*H on day 2 is associated with an increase in buffer base in all patients. The largest increase in buffer base (9 mEq./liter) occurred in case 4; the patient was given 133.8 mEq. of sodium bicarbonate intravenously between the studies on day 1 and day 2. None of the other patients was so treated but the increase in buffer base which they showed might be explained in part by the sodium load contained in the large volumes of ACD blood given during the surgical procedure.[8]

The elevation of arterial P_{CO_2} on day 1 seen in cases 2, 3, 5 and 6 indicates a minimal degree of hypoventilation. This finding does not correlate with the lowered arterial oxygen saturations and, with the exception of case 3, the return to a normal or low P_{CO_2} on day 2 is not accompanied by a return to a normal oxygen saturation. This suggests a slight and clinically insignificant disturbance in the distribution of blood and air in the lungs during the early postoperative period.

Comment

Current preference for the closed-chest perfusion technique is based primarily on the fact that thoracotomy and cannulation of the heart are not required. At the time this method was adopted, two potential disadvantages were apparent: (1) the relatively low flow rates resulted in longer perfusion times and possibly inadequate perfusion, and (2) the inability to decompress the left side of the heart created the potential hazard of trauma to the postarteriolar portion of the pulmonary vascular bed due to increased hydrostatic pressure. To the time of this writing, the closed-chest technique had been used on 28 patients, and no clear-cut clinical evidence had developed to suggest difficulties arising from the suggested potential hazards. It was the purpose of this study to clarify some of these problems, particularly in terms of the adequacy of perfusion and the effects of the technique on cardiac and pulmonary function.

The tendency toward metabolic acidosis on day 1, although mild in degree, indicates that

the flow rates utilized (1.1 to 1.7 liters/minute/m.^{2}) may not be totally adequate. The fact that the lowest values for buffer base occurred in the two patients who were exposed to prolonged periods of low flow (0.6 to 1.0 liter/minute/m.^{2}) at 15° C. emphasizes the importance of relatively high flows even at this temperature. This observation is supported by previous studies [5] on patients who underwent the open-chest technique and in whom a significant decrease in oxygen uptake at 15° C. was observed when the flow rates were decreased to less than 1.4 liters/minute/m.^{2}

The effect of the closed-chest technique on cardiac and pulmonary function would also appear to be mild in degree. In only one of the 5 patients studied did there appear to be any significant impairment of myocardial function. This patient, after correction of concomitant hypovolemia, made an uneventful recovery. Evaluation of postoperative pulmonary function was based only on P_{CO_2} and oxygen saturation. By these standards the degree of impaired pulmonary function was no greater than that reported after other surgical procedures.[9]

In a comparison of these data on the closed-chest technique with those obtained on patients undergoing the open-chest technique, certain observations are noteworthy. Similar slight degrees of impaired cardiac performance in the early postoperative period were noted after each technique. Patients in both the open-chest group and the closed-chest group showed some decrease in arterial oxygen saturation in the postoperative period although it was somewhat more significant in the open-chest group. This difference could be explained as the result of thoracotomy as well as by the fact that in the open-chest technique the lungs are actively ventilated throughout cooling and rewarming. Metabolic acidosis was not observed in the open-chest group and the authors of that work concluded, "Hypothermia per se does not produce metabolic acidosis provided adequate flow rates are maintained during perfusion." [5] The presence of mild metabolic acidosis in the closed-chest group supports this conclusion since the flow rates used probably were not totally adequate in all cases. Based on the physiologic data obtained in both these studies, no clear-cut preference for one technique is apparent in terms of postoperative cardiac, pulmonary and metabolic functions.

Several important questions regarding the closed-chest perfusion technique remain unanswered. No studies have been done in human beings to determine the levels of left atrial pressure or pulmonary wedge pressure during perfusion without cardiac function. Such data would be helpful in evaluating the overall risk of the procedure and the effectiveness of the various precautions taken to minimize buildup of left atrial pressure.[8] Likewise, no studies have yet been done to determine the effect of profound hypothermia on cerebral blood flow in man. The use of 7 per cent carbon dioxide during the cooling phase for the purpose of increasing cerebral blood flow is based on only indirect evidence in dogs and may well be unnecessary. Finally, no studies have been done at this institution to determine the usual acid-base profile and oxygen saturations subsequent to routine craniotomy. This information would be helpful in determining the significance of the changes observed in this study and in others. It is hoped that the answers to some of these questions will be available in the near future.

Summary

Postoperative physiologic studies were carried out in 6 patients after repair of intracranial aneurysm with the aid of profound hypothermia induced by a closed-chest perfusion technique. Hemodynamic studies indicated some impairment in myocardial function in one patient and hypovolemia in one patient; in 3 patients results were normal. Acid-base determinations showed a tendency toward metabolic acidosis on the evening of operation. This tendency probably was secondary to the comparatively low flow rates utilized for perfusion. Buffer base was lowest in the 2 patients who were exposed to prolonged periods of low flows at 15° C. Postoperative oxygen saturations of patients breathing room air were somewhat below normal, but clinically they were not significant. Comparison of these data with data previously obtained on patients cooled by an open-chest perfusion technique indicates little difference between the two

techniques in relation to postoperative hemodynamic, metabolic and pulmonary functions.

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References

1. MacCarty, C. S., Kirklin, J. W., and Uihlein, A.: The application of profound hypothermia to the treatment of cerebrovascular disorders, Ass. Res. Nerv. Ment. Dis. Proc., in press.
2. Terry, H. R., Jr., Daw, E. F., and Michenfelder, J. D.: Hypothermia by extracorporeal circulation for neurosurgery: an anesthetic technic, Anesth. Analg. **41**: 241, 1962.
3. Michenfelder, J. D., Kirklin, J. W., Uihlein, A., Svein, H. J., and MacCarty, C. S.: Clinical experience with a closed-chest method of producing profound hypothermia and total circulatory arrest in neurosurgery, Ann. Surg. **159**: 125, 1964.
4. Michenfelder, J. D., Terry, H. R., Jr., Daw, E. F., MacCarty, C. S., and Uihlein, A.: Profound hypothermia in neurosurgery: open-chest versus closed-chest techniques, ANESTHESIOLOGY **24**: 177, 1963.
5. Rehder, K., Kirklin, J. W., MacCarty, C. S., and Theye, R. A.: Physiologic studies following profound hypothermia and circulatory arrest for treatment of intracranial aneurysm, Ann. Surg. **156**: 882, 1962.
6. Payne, W. S., Theye, R. A., and Kirklin, J. W.: Effect of carbon dioxide on rate of brain cooling during induction of hypothermia by direct blood cooling, J. Surg. Res., **3**: 54, 1963.
7. Theye, R. A., Rehder, K., Quesada, R. S., and Fowler, W. S.: Measurement of cardiac output by an indicator-dilution method, ANESTHESIOLOGY **25**: 71, 1964.
8. Litwin, M. S., Smith, L. L., and Moore, F. D.: Metabolic alkalosis following massive transfusion, Surgery **45**: 805, 1959.
9. Nunn, J. F., and Payne, J. P.: Hypoxaemia after general anaesthesia, Lancet **2**: 631, 1962.

ALDOSTERONE BLOCKERS Influence of the aldosterone blocking agent aldactone on advanced respiratory insufficiency of chronic cor pulmonale has been studied in ten patients. Treatment with aldactone lasting seven to 14 days caused an increase in oxygen saturation, oxygen pressure and the *p*H in the arterial blood. Carbon dioxide pressure in the arterial blood and carbon dioxide content in plasma were significantly reduced. Reduction of renal blood flow regularly causes changes in aldosterone production. Changes in oxygen saturation have no direct influence on aldosterone production but lowering of the body *p*H stimulates it. This might be one mechanism to explain the surprising therapeutic effect of aldactone in the treatment of severe respiratory acidosis. Another possibility lies in the chemical affinity between progesterone and aldosterone. Progesterone has been known to be an antagonist to aldosterone and to stimulate respiration. Aldactone has also been shown to reduce cerebral edema within a few hours which also explains improvement of respiration. (*Hänel, J.: Aldactone Effect on the Advanced Respiratory Insufficiency (Respiratory Acidosis) of Chronic Cor Pulmonale, Muenchen Med. Wschr. 105: 2179 (Nov.) 1963.*)