MANAGEMENT AFTER CARDIAC ARREST*

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DEATH subsequent to initially successful cardiac resuscitation is not uncommonly reported. Fatalities are primarily related to central nervous system damage. Too often the cycle of hypoxia, cardiac arrect, circulatory arrest, central nervous system damage, cerebral oedema, hypoxia, becomes irreversible, despite successfully resuscitated cardiac and circulatory haemodynamics.

The introduction of deliberately induced controlled hypothermia and the availability of an intravenous urea preparation have provided the anaesthetist with two valuable adjuncts in the management of the patient after cardiac arrest. On a physiologico-pharmacological basis they are applicable to the problems of these patients. It is well documented that hypothermia reduces oxygen requirements of central nervous system tissues and allows their survival during reduced oxygen supply. This is desirable in patients with recent hypoxic trauma to the central nervous system. Urea has been shown to reduce cerebral spinal fluid pressure and cerebral oedema. These two techniques, then, would appear useful in the reversal or arrest of the grave hypoxic cycle, permitting time and conditions for recovery of hypoxic damage to central nervous system tissues. We have had this hypothesis substantiated by our clinical results.

Table I summarizes six selected case reports, illustrating the beneficial application of these principles, as a guide to a method of management of patients after cardiac arrest.

TABLE I

CLINICAL SUMMARY OF PATIENTS AFTER CARDIAC ARREST

Case	Inadequate Perfusion (mins.)	Neurological Sequelae	Management	Result
1	4+	Nil	Nil	Recovery
2	3+	Nil	Hypothermia	Recovery
3	2+	Unconscious Dilated Pupils Convulsions	Hypothermia (late)	Death
4	4+	Nil	Urea	Recovery
5	4+	Unconscious Convulsions	Hypothermia Urea	Recovery
6	4+	Unconscious	Hypothermia Urea	Recovery

*Presented at the Annual Meeting, Canadian Anaesthetists' Society, May 15-18, 1961.
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Case I

Age 58 years. Craniotomy for acoustic neuroma—sitting position. Cardiac arrest occurred owing to air embolus. The patient was changed to the supine position and a thoracotomy confirmed diagnosis of cardiac arrest. Following cardiac massage spontaneous heart action resumed. The period of arrest was approximately 4–5 minutes. After closure of the thoracotomy the pupils were normal, respiratory effort adequate and the patient was responding to painful stimuli. On return to the recovery room, there were no demonstrable neurological sequelae and the patient made an uneventful recovery.

Case II

Age 13, for lumbo-sacral laminectomy—prone position. Cardiac arrest occurred 13 minutes after induction. Thoracotomy proved the diagnosis and massage was started within 3 minutes. After 29 minutes, following electrical defibrillation, Ca gluconate, and intracardiac epinephrine, blood pressure was maintained at 110/80.

Because of the prolonged resuscitation period with its associated cerebral hypoxia, hypothermia was initiated as the thoracotomy was closed. Temperature was maintained at 28–32° C. for 24 hours. This patient did not receive any urea preparation as it was not available at this time. The patient made an uneventful recovery.

Case III

Age 27, for Caesarean Section. After the delivery of the placenta the surgeon noticed lack of bleeding in the wound and the anaesthetist became aware that there was no blood pressure. Immediate thoracotomy confirmed the diagnosis of cardiac asystole in an estimated 2 minutes.

The heart was flabby but responded rapidly to massage and calcium injection. The patient's pupils were dilated but returned to normal in the recovery room. Because of a slow return to consciousness hypothermia was begun 5 hours after arrest. Despite continuous low temperature and sedation, convulsive seizures occurred and persisted. The patient succumbed 5 days later.

Case IV

Age 44, for abdominal hysterectomy. The patient developed hypovolemia owing to haemorrhage. Carotid pulsation was absent, the blood pressure was zero and the pupils dilated. Thoracotomy confirmed arrest and massage was started in approximately 4 minutes. Within 15 minutes of arrest the blood pressure maintained at 100/80. The patient was given 70 gm. of urea intravenously over a 1-hour period. As the thoracotomy was being closed the pupils were small and reacting, the patient was breathing spontaneously, swallowing and coughing on the endotracheal tube. One hour later the patient was responding to commands. The patient was returned to the recovery room and observed for neurological sequelae. Because of her satisfactory status and no pyrexia over 101° by rectum, further treatment was withheld. The patient made an uneventful recovery.

Case V

Age 47 years, for vaginal repair. Arrest of circulation was first noted by the surgeon at the operative site. Thoracotomy verified cardiac arrest. Effective circulation was restored in approximately 4 minutes by cardiac massage. Since asystole must have been preceded by a period of severe hypoxia and because of a sluggish return of consciousness and an associated pyrexia, hypothermia was begun immediately, to 28–30° C. This temperature was maintained for 72 hours. During rewarming the patient exhibited major convulsive seizures. At this time the patient was given intravenous urea and cooling to 30° C. was resumed. Sedation at this time was augmented by phenobarbital and diphenylhydantoin sodium (Dilantin®). This temperature was maintained for a further 24 hours, when the patient was rewarmed with subsequent uneventful recovery.

Case VI

Age 49, for hysterectomy. Shortly after the skin incision the blood pressure was not recordable. Thoracotomy was performed within 3–4 minutes. The heart was in asystole. It responded quickly to massage but the blood pressure remained low (40–50 systolic) for 30 minutes despite calcium and vasopressors. After 30 minutes the blood pressure was 80/40 and the chest was closed. Three hours post-arrest, owing to a slow return to consciousness the patient was sedated and cooled. Four hours post-arrest, intravenous urea was administered. The temperature was maintained at 28–30° C. for 24 hours. Following rewarming the patient made an uneventful recovery.

Method

The initial treatment of cardiac arrest, namely, the method of cardiac resuscitation has been described elsewhere.[1] It is the immediate and prolonged post-arrest care which is to be described here.

These six cases have been selected as representative of groups of patients who have been treated in various ways. From this experience our present methods have evolved, as outlined in Table II.

TABLE II

MANAGEMENT AFTER CARDIAC ARREST

1	Urea—I/V 1 gm./Kg.	
2	Hypothermia, 28°–30° C.	
3	Sedation	
	(i) Demerol—0.04%	I/V
	(ii) Phenergan—0.01%	
	(iii) Phenobarbital	I/M
	(iv) Dilantin	
	(v) Pentothal—2.5%	I/V
	(vi) Paraldehyde	I/M

Definitive post-arrest management is formulated according to the progress of the initial resuscitation. Cardiac problems seldom arise following successful resuscitation and it is to the central nervous system that our attention is directed.

First to be considered is the probable duration of inadequate circulation. This may be difficult to assess, as the cessation of circulation may be preceded by a period of hypoxia. If at this stage it appears that the cerebral circulation has been inadequate for a period of 4 minutes or more it is considered advantageous to start an intravenous infusion of urea preparation (1 gm./Kg.).

In the event of a rapid cardiac response with a period of inadequate circulation known to be less than 4 minutes, urea may be withheld. However, the side effects of urea are negligible and its early use so advantageous that it is perhaps unwarranted to deprive the patient of its potential benefit.

As soon as cardiac function has been restored and the thoracotomy is being closed the patient is assessed for neurological deficits. At this time neurological sequelae may be manifest by dilated pupils, slow return of spontaneous respirations or a slow return to consciousness. If there is any evidence of such neurological damage the patient's temperature is rapidly lowered to 28–30° C. by means of a circulating blanket (Thermorite®) and maintained at this level for

48–72 hours or until there is no further evidence of central nervous system damage. It may be necessary to rewarm gradually in order to assess the neurological situation.

If the arrest or the resusciation has been prolonged, the patient's temperature is lowered without waiting for any actual evidence of damage. In the absence of prolonged resuscitation, or if the arrest period is estimated to be under 4 minutes, hypothermia is withheld until some evidence of central nervous system damage develops. This evidence may take the form of hyperpyrexia (over 101° F. by rectum), or the first signs may be twitchings or convulsive seizures.

In order to initiate hypothermia these patients are sedated with intravenous meperidine .04 per cent and promethazine 0.01 per cent (Demerol® 200 mg., Phenergan® 50 mg. in 500 cc.). This sedation may be given rapidly enough to prevent shivering, but not so quickly as to depress the respiratory or cardiovascular activities to dangerous levels. In our experience it has not been necessary to use chlorpomazine to facilitate rapid cooling and the hypotension characteristically produced by this drug has been avoided. Further sedation is added in the form of intramuscular phenobarbital and dilantin sodium, which act synergistically to reduce shivering and control convulsions. The dilantin also acts to prevent ventricular arrhythmias which may occur during hypothermia. These drugs are given q.4.h. and as the level is increased in the tissues the administration of meperidine-promethazine solution may be reduced. If convulsions become troublesome they may be controlled by small repeated doses of intravenous thiopentone 2.5 per cent. For long-term control of these convulsions, intramuscular paraldehyde may also be used.

Careful nursing care is all-important. The patient should be moved carefully. Antibiotics are used to minimize the possible development of hypostatic pneumonia. By close attention to detail the temperature may be maintained at a given level, the patient may be adequately sedated without depression and fluid balance and electrolyte levels may be maintained.

If the period of anoxia has been lethal, convulsions appear and persist despite sedation and low temperatures. However, the use of intravenous urea, hypothermia and adequate sedation as described, seem to offer the best opportunity to date for recovery.

Discussion

The Central Nervous System shows less tolerance to lack of oxygen than any other organ system because of its complete dependency on aerobic energy production from glucose. Bedford[2] stresses that four minutes of anoxia is the maximum limit for cortical cell survival and ten minutes the outside limit for any nerve element survival at all.

It is agreed that prognosis is often difficult to judge because the duration of cerebral hypoxia is usually not known, but several articles[3,4,5] mention that pupillary dilatation, vasomotor instability, sweating and a flat or file pattern E.E.G. denote a grave prognosis.

In our experience, neurological sequelae such as persistent dilated pupils, slow return to consciousness and recurring convulsions are indications of a

grave prognosis, unless active therapy of the type outlined is begun early. The E.E.G. has not proved useful as a guide to prognosis in our series. The death of the patient in Case III, demonstrating these neurological sequelae, in which hypothermia was not begun until five hours post-arrest, illustrates this concept forcefully.

It has been realized since 1927 that urea was effective in reducing cerebrospinal fluid pressure in animals, but it was not entertained seriously in clinical application until 1956. Javid[6] summarized an experience of 300 administrations, attesting to its dependability and freedom from side effects in promoting reduction in intracranial, intraorbital and spinal cord volumes.

Benson[7] cites the Central Nervous System features consequent upon hypoxic damage, with its resultant increased tissue permeability, secondary brain swelling and increase in volume with consequent brain stem herniation, cerebrospinal fluid obstruction, further neurone damage and midbrain haemorrhage and further local ischaemia. There is no doubt that urea can favourably affect this cycle of events. This point is well illustrated in our Cases IV and V where urea proved useful in the prevention and control, respectively, of convulsions due to secondary oedema.

Hypothermia offers many advantages in treatment of these problems. Not only has hypothermia proved useful in the management of convulsions and unconsciousness in these patients, as in Cases V and VI, but it is also an invaluable adjunct to the control of the neurological manifestation of pyrexia, as our Case V demonstrated. It has been shown that hypothermia not only reduces brain volume, but also reduces cerebral oxygen consumption and blood flow. Rosomoff *et al.* have produced experimenal results illustrating these features.[8,9,10,11] As temperature is reduced there is a reduction in cerebral metabolism of 6.7 per cent per degree C. of pre-cooling value, with a corresponding decrease in cerebral blood flow over the range 35–25° C. As a result the A V oxygen differences are unchanged.[8] Mean Blood Pressure is also reduced by 4.8 per cent per degree C., over a similar temperature range.[8] Cerebrovascular resistance is increased and brain volume decreased during hypothermia so that at 25° C. the brain size is decreased by 4.1 per cent, while the extracerebral space (i.e., space unoccupied by brain) is increased 31.8 per cent.[10] Rosomoff[10] also found cerebrospinal fluid pressure and venous pressure to be reduced at a rate of 5.5 per cent per degree centigrade.

Myocardial anoxia of varying degrees, resulting in conduction disturbances, occasionally is present in these patients, but is seldom the cause of their demise. Our experience has shown the efficacy of diphenylhydantoin sodium (Dilantin®) in such problems. These findings are being presented in a separate report. Not only does the small volume of published data attest to its value in the treatment of ectopic arrhythmias[13,14,15] but the anti-convulsant properties of the agent can be of value in treatment of the post-anoxic patient, as was also demonstrated in our Case V. It is suggested[13,14,15] that the toxicity of Dilantin® is no greater than procaine amide (Pronestyl®) and probably less than that of procaine HCl or quinidine.

The clinical use of urea and hypothermia is being rapidly extended at the

present time. There is little doubt that both of these therapeutic measures cause a reduction in cerebral volume. Hypothermia, in addition, results in a decrease of cellular metabolism and cerebral blood flow. The relationship of cerebrospinal fluid pressure to haemodynamic factors in normothermia and hypothermia is not yet resolved.[11] Rosomoff *et al.*[16] have shown that hypothermia protects against experimental brain injury if instituted to 25° C. within 3 hours of injury.

The results of the experimental laboratory, when correlated with an increasing volume of clinical appraisals, certainly suggest that there is indeed a rational basis for the use of these techniques and agents to reduce oedema and cellular metabolism immediately after the traumatic episode.

Summary

On the basis of six selected cases from a larger clinical series, a method of management after cardiac arrest has been described. Fatalities are primarily related to central nervous system damage. Clinical manifestations of this damage present as neurological sequelae such as hyperpyrexia, persisting unconsciousness, dilated pupils, absence of spontaneous respirations and convulsions. The use of intravenous urea (1 gm./Kg.) and deliberately induced, controlled hypothermia has been valuable in the prevention of irreversible central nervous system damage. The judicious use of sedative agents such as meperidine, promethazine, phenobarbital, diphenylhydantoin sodium, thiopentone and paraldehyde has been shown to be a valuable adjunct to hypothermia and in control of convulsions.

Résumé

Nous avons choisi six cas parmi un grand nombre de cas cliniques et nous traçons une ligne de conduite à suivre à la suite d'un arrêt cardiaque. Les mortalités sont attribuables en premier lieu à des lésions du système central. Comme manifestations cliniques, ces lésions produisent des séquelles neurologiques, telles que l'hyperthermie, l'inconscience prolongée, des pupilles dilatées, l'absence de respiration spontanée et des convulsions. Pour prévenir l'irréversibilité des lésions du système nerveux central, nous croyons avantageux d'employer de l'urée par voie endoveineuse (1 grm/Kg) et de provoquer une certaine hypothermie. Pour combattre les convulsions et comme adjuvants à l'hypothermie, il nous a semblé indiqué de recourir à l'usage judicieux de sédatifs tels que la mépéridine, la prométhazine, le phénobarbital, le dilantin, le thiopentone et le paraldehyde.

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