ALTHESIN THERAPY – AN ADJUNCT FOR INTRACRANIAL PRESSURE CONTROL REGIMES? – A PRELIMINARY REPORT

A. E. DELILKAN
M. NAMAZIE

SUMMARY

A retrospective report (1970 - 1980) on patients (non-head injuries and head-injuries) admitted with cerebral ischaemia into the intensive therapy unit is presented.

The principles of management to reduce and control intracranial pressure are outlined.

Since 1978 continuous intravenous infusion with Althesin has been used instead of barbiturates in the regime. Mortality rate fell from 83.7 percent (1970 - 1977) to 43.7 percent (1978 - 1980) for non-head injury patients and from 72.1 percent (1970 - 1977) to 45.6 percent (1978 - 1980) in the head-injured group, the differences between the periods being statistically significant. The possible influencing factors are mentioned. The quality of salvage and survival requires investigation.

INTRODUCTION

Cerebral ischaemia occurs whenever there is a reduction or cessation of blood flow in the brain or when there is direct local intracranial damage. Another approach to cerebral ischaemia is to divide the causation of cerebral ischaemia into two broad categories – post-cardiorespiratory arrests (non-head injuries) and intracranial trauma. The common factor in these two categories is the significant degree of brain damage that occurs secondarily following the initial insult. It is the sequel of cerebral ischaemia, whatever the antecedent cause, that is preventable and thus requires a common regime of cerebral protection to contain the expected rise in intracranial pressure (I.C.P.) with its deleterious effects.

This paper is a retrospective review of patients with cerebral ischaemic episodes (post-cardiorespiratory arrests and head-injuries) treated in the Intensive Therapy Unit, University Hospital, Kuala Lumpur during the period 1970-1980. Since 1978 continuous Althesin infusion therapy has been introduced as one of the components of the regime to control intracranial pressure.

MATERIALS AND METHOD

From 1970 - 1980, 763 patients were admitted to the intensive care ward with cerebral ischaemia (620 with cardiorespiratory arrest following cardiac infarction, problems during and/or immediately after anaesthesia/surgery, acute non-surgical central nervous system disorders and 143 head-injured patients). See Tables I and II.

The regime of management (during 1970 - 1977) for these patients (509) basically was as follows:

Hyperventilation was achieved by intermittent positive pressure ventilation facilitated by administering neuro-muscular blockers, maintaining the PaCO$_2$ around 3.3 - 4.0 kPa (25-50 mm Hg). Pharmacological agents (mannitol or frusemide therapy) with fluid restriction was used.
to reduce cerebral oedema. Intraventricular catheter insertion provided an avenue for release of cerebrospinal fluid if indicated. Dexamethasone was administered empirically to reduce cerebral oedema though its value in the head injured patients is not conclusive. Some patients received diazepam, some barbiturates while others did not receive any drugs for the purpose of central nervous system depression. Surface cooling (aided by electric fans) was used to maintain a temperature of 31 - 33°C.

The monitoring used in these cases were a pupil size and reaction, pulse rate and blood pressure measurement every 15 minutes – 2 hours. Continuous E.K.G. was displayed, urine output was measured hourly and arterial blood gases analysed at least twice a day.

From 1978, 254 patients with cerebral ischaemia (non-head injuries and head injuries) were managed in the intensive care ward. The regime used was basically the same except that continuous intravenous infusion of Althesin (0.1 - 0.2 ml/kg/hour) was used as the method for central nervous system depression.

The additions to monitoring (from 1978) included continuous intra-arterial blood pressure display, continuous intra-cranial pressure display for up to 72 hours via an intraventricular line connected to a transducer and oscilloscope.

Non-Head Injuries

Three hundred and fifty-four out of 423 patients (non-head injury cerebral ischaemia) died (83.7 percent mortality or 16.3 percent salvage) during the period (1970 - 1977) before continuous Althesin therapy was included in the management of these patients. Since the introduction of Althesin therapy (1978 - 80) 86 out of 197 patients died (43.7 percent mortality or 56.3 percent salvage). Chi-square tests showed that the mortality difference between the two periods was statistically highly significant (p < 0.001).

Head Injuries

Before Althesin therapy (1970 - 1977) there were 62 deaths out of 86 patients (72.1 percent mortality or 27.9 percent salvage). Since the introduction of Althesin therapy (1978 - 80) 26 out of 57 patients died (mortality 45.6 percent or salvage 54.4 percent). Chi-square tests showed that the difference between the mortality rates of the two periods was statistically significant (p < 0.01).

DISCUSSION

The action and value of barbiturate therapy in protecting the brain against the effects of cerebral ischaemia.

### Table I

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<td>50</td>
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<td>(81.9)</td>
<td>(85.1)</td>
<td>(77.4)</td>
<td>(69.5)</td>
<td>(50.8)</td>
<td>(42.6)</td>
<td>(37.9)</td>
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Footnote: There was no neurosurgeon in the University Hospital, Kuala Lumpur in 1976, 1977.

### Table II

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<td>8</td>
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<td>(%)</td>
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Footnote: There was no neurosurgeon in the University Hospital, Kuala Lumpur in 1976, 1977.
ischaemia is well known both in experimental work and in therapeutic management of such patients. Barbiturates reduce cerebral metabolic requirements for oxygen (CMRO2) and cerebral blood flow. These effects reduce intracranial pressure. Barbiturates with hypothermia form a beneficial combination to reduce and control I.C.P.; gamma-hydroxybutyrate and its lactone, aspartate, glutamine, oxaloacetate and aminophylline are other pharmacological agents which have been shown to have beneficial effects in experimental cerebral ischaemia. Recently (1980) Belopavlovic and Buchthal have reviewed and reported on the use of barbiturate therapy in the management of cerebral ischaemia. In our intensive therapy unit since 1978 Althesin has been used in place of barbiturates on the same principles in the regime of management for control of intracranial pressure for the first 72 hours following cerebral ischaemia. Althesin has been shown to have similar effects as barbiturates in reducing CMRO2, in reducing cerebral blood flow and cerebrospinal fluid pressure. Being an intravenous general anaesthetic drug Althesin does produce unconsciousness and thus removes the response to environmental stimuli which would otherwise provoke a rise in intracranial pressure. It has also been used to control convulsions as with barbiturates which adds to its beneficial role in the management of intracranial problems.

The advantage of Althesin over barbiturates in the management of cerebral ischaemia is that the former is short-acting (the drug is rapidly metabolised in the body) with a quicker recovery; this feature of Althesin allows for easier periodic neurological assessment of the patient on stopping the infusion; it has been reported that after 20 days of continuous Alphaxalone-Alphadolone (Althesin) intravenous infusion neurological assessment was possible 12 minutes after stoppage. With our dosage of 0.1 - 0.2 ml/kg/hr. Althesin infusion in Malaysian patients neurological assessment is possible within 30 minutes. Stopping barbiturate therapy for periodic neurological assessment is more inconvenient and difficult because of the lingering "hang-over" effect caused by the redistribution property of barbiturates within the body. As with barbiturates, Althesin therapy can depress the cardiovascular system and must thus be used cautiously and might require the addition of ionotropic drugs in circulatory depressed states. No statistical significance can be derived from the results of this retrospective study: there is insufficient evidence that the two groups of patients (1970 - 77 and 1978 - 80) were strictly comparable.

The obvious improved salvage rate (reduced mortality) achieved since the introduction of Althesin for the management of cerebral ischaemia could have been influenced, obviously, by more than one factor. General improvement in patient-care (more nursing personnel, twenty-four hour residential cover by anaesthetic staff in the ward, better monitoring equipment etc.) since the reorganisation of the intensive care unit in 1978, has been seen in the overall results obtained (1970 - 1977: total admissions 2295, deaths 462 i.e. mortality 20.1 percent, 1978 - 1980: total admissions 1611, deaths 245 i.e. mortality 15.2 percent).

In the management of cerebral ischaemia besides achieving better salvage rates, the quality of survival is equally, if not more, important. Improved quality of survival is dependent on the underlying pathology, the antecedent cause, the speed with which resuscitation is commenced, the speed with which definitive therapy is settled and the standard of intensive care therapy provided. An aggressive attitude towards cerebral resuscitation as practised in the intensive care ward, University Hospital, Kuala Lumpur, will always carry the possibility of salvaging life but producing the vegetative state and brain death. While it is justified to save life, is it justified to prolong death? The quality of survival is the crucial factor and this long-term evaluation will have to be done.

ACKNOWLEDGEMENTS
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REFERENCES


