THE PHENOMENON OF HYPOXIC BRAIN DAMAGE AT KENYATTA NATIONAL HOSPITAL INTENSIVE CARE AND HIGH DEPENDANCY UNITS

A DISSERTATION SUBMITTED IN PART FULFILLMENT FOR THE REQUIREMENT OF THE DEGREE OF MASTER OF MEDICINE (ANESTHESIA), UNIVERSITY OF NAIROBI.

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TITLE

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DECLARATION

This thesis is my original work and to my knowledge has not been presented for a degree in any other university.

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God for giving me the strength and availing the resources and friends

DEDICATION

"For we are not of those who shrink back and are destroyed but of those who believe and are saved."

Heb 10:37

To all the people who have or have ever had a patient with Hypoxic Brain Damage, we do not shrink back but press on.

To all the Medical workers who work hard in trying to prevent it, Gods' strength and wisdom.

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ABBREVIATIONS

ICU	Intensive Care Unit
HDU	High Dependency Unit
KNH	Kenyatta National Hospital
SHO	Senior House Officer
HBD	Hypoxic brain damage
ABGA	Arterial blood gas analysis
Hb	Hemoglobin concentration
RBG	Random blood glucose
CTScan	Computer Tomography Scans
CA	Cardiac arrest
RA	Respiratory arrest
O_2	Oxygen
EEG	Electroencephalogram
kPa	Kilopascals
CPR	Cardiopulmonary resuscitation
CPCR	Cardiopulmonary cerebral resuscitation
PVS	Persistent vegetative state
GCS	Glasgow Coma Scale
PaO_2	Arterial partial pressure of oxygen
$PaCO_2$	Arterial partial pressure of carbon dioxide
pH	Logarithm of the concentration of hydrogen ions
SaO_2	Arterial saturation of oxygen

FIO_2	Fraction of inspired oxygen
MAP	Mean arterial pressure
SBP	Systolic blood pressure
PEEP	Positive end-expiratory pressure
ECG	Electrocardiogram

SUMMARY

Information relating to twelve patients admitted into the Kenyatta National Hospital Intensive Care and High Dependency Units with a primary diagnosis of Hypoxic Brain Damage, was analyzed. The range of ages was from one-day-olds to adults and the length of stay within the units varied from one to nine days with an average stay of three days.

Eight (66.7%) of the patients were admitted from operating theatres within or outside of Kenyatta National Hospital, while the remaining four (33.3%) were from the casualty. All twelve patients were resuscitated prior to admission either as a result of cardiac arrest (33.3%) or respiratory arrest or failure (66.7%). The duration of resuscitation was only indicated in one (8.3%) of the cases with the duration of resuscitation being five minutes. On admission to the units, three (27.3%) of the patients were hypotensive, one patient (8.3%) was bradycardic and six patients (50.5%) were hypothermic.

Investigations done on the patients while in the units included arterial blood gases on all cases; random blood sugar in eleven cases (91.7%), hemoglobin levels in five cases (41.7%), serum sodium and potassium levels in ten (83.3%) and eleven (91.7%) cases respectively. Computer Tomography Scans of the brain were not done on any of the patients.

Neurological assessments were done on all the twelve patients on admission. Ten (83.3%) of the patients had a Glasgow Coma Scale of 3 out of 15, one (8.3%) had a scale of 4 out of 15, one patient was not assessed as the patient was paralyzed and sedated with a neuromuscular blocking agent and a benzodiazepine

respectively. Pupillary light reflex assessment on admission revealed three patients (25%) had response to light while nine (75%) patients had no response to light. Of the latter, five (41.7%) had mid-dilated pupils and four (33.3%) fully dilated pupils.

Management of patients included antibiotic therapy and mechanical ventilation in eleven cases (91.7%), ionotropic support in one case (8.3%) and steroid therapy in four cases (33.3%). Eleven (91.7%) of the patients died while in the unit while one (8.3%) was transferred to the wards. An assessment for brain death was made in only four (33.3%) of the patients.

INTRODUCTION

Hypoxic Brain Damage (HBD), otherwise referred to as Hypoxic/Anoxic-ischaemic Encephalopathy (H/AIE), is one of the conditions that necessitate admission into the Kenyatta National Hospital Intensive Care and High Dependency Units (KNH ICU/HDU). HBD is associated with high morbidity and mortality than many other conditions seen in Intensive Care Units. Patients admitted with HBD may have varying degrees of brain damage, depending on the severity of the initial insult to the brain.

This study was a retrospective, descriptive, cross-sectional survey that was undertaken with regard to all patients admitted to the KNH ICU/HDU with a diagnosis of HBD between the period of 1st January 1995 to 31st December 1999. The study describes the phenomenon of HBD in patients over this five-year period and examines associations between HBD and other variables. An important variable is any event that may lead to a reduction in blood flow or oxygen supply to the brain in the patient prior to admission to the units. Such events could include a hypotensive episode, cardiac and/or respiratory arrest. Any resuscitative measures performed on the patient prior to admission were documented in detail and analyzed.

Information collected during the patients' stay in the ICU/HDU on neurological status, including the Glasgow Coma Scale, cortical, brain stem and motor function, was synthesized. Particular attention was taken to note changes in neurological condition during patient's stay. Documentation was also collected on the patients'

vital signs on admission. The findings from any investigations undertaken, such as arterial blood gases, hemoglobin level, random blood sugar and any computer tomography scan results were recorded. In addition, information on the management, length of stay in the ICU and the final outcome of any patient admitted with a diagnosis of HBD was collected. Finally, the study investigated whether critical evaluation of the severity of brain damage and the moribund status of patients' was determined during their stay in the ICU.

A detailed discussion has been presented on the phenomenon of HBD at KNH with important conclusions and recommendations.

LITERATURE REVIEW

BACKGROUND

Modern cardiopulmonary resuscitation (CPR) is based on ideas conceived or accidentally discovered over at least four centuries. These ideas were then re-discovered, re- explored and synthesized into an effective resuscitation system in the 1950's and 1960's, before which there were few immediately applicable effective emergency techniques available. Modern respiratory resuscitation was pioneered in the 1950's; external cardiac resuscitation in the 1960's; and cerebral resuscitation after cardiac arrest in the 1970's, when CPR was extended to Cardiopulmonary-Cerebral Resuscitation (CPCR) (*1,2*). Recognizing that brain resuscitation is an important part of any successful resuscitation has led to the CPCR system of basic, advanced and prolonged life support as we know it today.

The human brain is a complex organ. It consists of some 10 billion neurons each with multiple axonal and dendritic connections to other cells controlling many important bodily functions. Although it represents only 2% of body weight, because of it's high metabolic activity, it receives 14% of the body's cardiac output (750 ml/min) and accounts for 18% of the body's oxygen use (46ml/min)(*1*). The oxygen consumption by the human brain (cerebral metabolic rate for O_2) averages approximately 3.5mL/100 g of brain/min.

As a result of this high metabolic rate and its relative inability to sustain anaerobic metabolism, the brain is extremely sensitive to hypoxia, and occlusion of its blood supply produces unconsciousness in as short a period as 10 seconds. If anoxia persists beyond 3-5 min, cerebral damage that may be permanent occurs. The

vegetative structures in the brain stem are more resistant to hypoxia than the cerebral cortex, and patients may recover from accidents such as cardiac arrest and other conditions causing fairly prolonged hypoxia with normal vegetative functions but severe, permanent intellectual deficiencies. The basal ganglia use oxygen at a very high rate, and symptoms of Parkinson's disease as well as intellectual deficits can be produced by hypoxia. The thalamus and the inferior colliculus are also very susceptible to hypoxic damage (3).

The various cellular elements in the nervous system have different susceptibilities to hypoxia. In general the nerve cells are the most sensitive, followed by oligodendroglia and astrocyctes, while the microglia and cellular elements of the vessels are least vulnerable (5).

CATEGORIES OF BRAIN HYPOXIA

These have been classified by Brierly (22) as follows:

Stagnant Hypoxia

Ischaemic - results from local or generalized arrest of cerebral blood flow. Localized ischaemic damage occurs if blood flow through an artery or one of its branches is arrested resulting in ischaemia to the area of the brain supplied by the affected vessel. Generalized ischaemic brain damage occurs more commonly following cardiac arrest resulting in global cessation of cerebral blood flow.

Oligaemic – this is due to reduction in blood supply to some or all parts of the brain. Localized reduction of blood flow in a single cerebral artery or one of its branches usually occurs from a combination of systemic hypotension and narrowing

of the vessel itself. A localized area of tissue necrosis ensues. Thus, HBD may then occur along the arterial boundary zones (watershed areas) of the cerebral and cerebellar hemispheres if a considerable generalized reduction in cerebral perfusion pressure occurs (*5*).

Anoxic and Hypoxic Hypoxia

Anoxic – results from absence of O_2 in the lungs, which leads to hypoxaemia. Blood leaving the lungs may be devoid of O_2, such as in drowning or complete obstruction of the respiratory tract above the tracheal bifurcation. The physiological events have been studied in man (*25, 26*). It is evident from these studies that pure hypoxaemia is complicated by some degree of circulatory failure within that period of time and therefore cannot, *per se*, produce brain damage. If resuscitation is successful and brain damage is eventually proved, this must be ascribed to a combination of hypoxaemia and some reduction in cerebral blood flow. Thus any delineation of purely anoxic brain damage is not as yet justified (*22*).

Hypoxic – this implies some reduction in the oxygen tension of arterial blood from reduction of O_2 content of inspired air, inhalation of O_2 mixed with inert gases during anesthesia or impairment of pulmonary function. The effect of graded hypoxia on the brain has been studied using a modified mechanically ventilated preparation rat. A reduction in arterial partial pressure of oxygen (PaO_2) to 3.7 kPa for 30 min produced moderate change in the energy state of brain tissue, whereas a reduction in PaO_2 to 2.8 kPa again for 30 min showed an abnormal energy state with persistent lactic acidosis and more extreme brain damage (*6*). Using a similar model in sub-human primates, Brierly *et al* (*5*) found that PaO_2 could be reduced to 4.7

kPa without affecting either brain metabolism or function. It was not until PaO_2 had been reduced to 2.8-3.2 kPa for at least 8 min that the electroencephalogram (EEG) became isoelectric and irreversible hypoxic brain damage (HBD) resulted.

Therefore, it is evident that brain damage can occur from acute complete deprivation of oxygen or from exposure to low oxygen tension for long periods of time. It must be noted that the pattern of brain damage in hypoxaemia is indistinguishable from that seen after oligaemia (*5*) emphasizing the fact that systemic hypoxia can only produce brain damage secondary to cardiac failure or arrest with associated reduction in cerebral perfusion pressure.

Anemic Hypoxia

This results from reduced hemoglobin content such as occurs in blood loss or anemia. Poisoning by carbon monoxide, however, reduces the amount of circulatory hemoglobin available to combine with O_2 and represents the only example of anemic hypoxia that is apparently capable of producing hypoxic changes in the brain (*5*).

Histotoxic Hypoxia

Poisoning of neuronal respiratory enzymes results in failure to utilize O_2 although the oxygen tension and content of arterial blood are normal (*5*).

CAUSES OF HYPOXIC BRAIN DAMAGE

Hypoxia or anoxia resulting in brain damage can occur following either cardiac and or respiratory failure, though more commonly from cardiac failure and arrest. This cardiac arrest may be primary or secondary (*2*). A summary of the more frequent causes of Cardiac arrest and possibly the most common causes of HBD is outlined below:

1. Primary:

- Ventricular fibrillation from focal myocardial ischaemia
- Ventricular fibrillation and asytole from myocardial infarct
- Heart block
- Electrical shock
- Drugs e.g. digitalis intoxication
- Heart failure from primary heart muscle disease e.g. dilated cardiomyopathy

2. Secondary:

- Rapidly developing e.g. asphyxia from airway obstruction or apnea, rapid blood loss and alveolar anoxia (from acute pulmonary edema or inhalation of oxygen-free gas)
- Slowly developing e.g. severe hypoxaemia (from pneumonia or pulmonary edema and consolidation, i.e. shock lung); oligaemia or distributive (septic) type shock; acute brain insults (leading to medullary failure and severe intractable hypotension and apnea)

Cardiac arrest can also be associated with anesthesia management in this order of incidence (*2*):

- Airway obstruction-hypoventilation-apnea
- Regurgitation and aspiration
- Relative overdose of myocardial depressant anesthetics (general as well as local anesthetics)
- Uncontrolled or unreplaced blood loss

- Uncontrolled hypotension from total sympathetic block secondary to spinal or epidural anesthesia

Cardiac arrest following anesthetic accidents may contribute up to 32% of the incidence of hypoxic brain damage (encephalopathy) (*10*). It can therefore be appreciated that irreversible brain damage can occur as a consequences of such diverse conditions as lung and heart disease, shock, seizures or any episodes leading to severe hypotension, and is a potential hazard to all patients with these conditions.

SIGNS AND SYMPTOMS OF HYPOXIC BRAIN DAMAGE

Signs and symptoms of HBD are related to the areas of the brain affected and may be divided into cognitive and physical deficits (*4*). Cognitive deficits include short-term memory loss, which is by far the most common and virtually universal symptom of HBD. The Hippocampus, the area of the brain critical for learning new information, has neurons that are highly sensitive to anoxia. Other cognitive deficits include anomia and visual disturbances, and in rare instances cortical blindness (Anton's Syndrome).

Among the physical deficits common symptoms include ataxia, aprasia, spasticity, paraparesis and even quadriparesis.

Long-term consequences of HBD include persistent coma or stupor, dementia, visual agnosia, Parkinsonism, choreoathetosis, cerebellar ataxia, and myoclonus (*4*). It is difficult to judge clinically, soon after cardiopulmonary cerebral resuscitation following cardiac arrest, the precise degree of brain damage secondary to

hypoxia/ischaemia, as the encephalopathy may mature over a period of a few days (*7*). It must be emphasized however that only prolonged global brain ischaemia results in brain death (*7*). A study done in KNH ICU showed that cerebral anoxia contributed to 10% of all patients found to be brain dead in the ICU (*32*).

EVALUATION

Although routine neurological examination of patients' one hour after cardiac arrest appears important (*11*), neurological recovery remains in doubt in the early postcardiac arrest state. However, management of the patient and advice to the relatives depends on assessments made during this period. Thus a criterion to gauge outcome is important. The more common criteria (*12*) that have been used are:

- Duration of anoxia
- Duration of post anoxic coma
- The Electroencephalogram (EEG); and
- Clinical examination of the neurological status

It is generally considered that the duration of anoxia is the best indicator of outcome, but in practice it is rare for the exact duration of anoxia to be known. Any accurately timed anoxic period is also likely to be brief as immediate resuscitative action is normally taken, and survivors do not usually constitute a prognostic problem. If cardiac arrest is of abrupt onset and occurs in a patient at normal body temperature, clinical recovery is unlikely if period of arrest exceeds 5-7 min, with many patients dying within 24 hours of arrest (*22*).

The exact duration of the post-anoxic coma is impossible to predict and most major decisions are made while the duration is still unknown. However, it has been found that in 90% of patients whose postanoxic coma lasted less than 48hrs, clinical recovery was complete (11).

The electroencephalogram (EEG) has been used most successfully to predict outcome but is impracticable to perform routinely in the ICU. Portable EEG machines can be used in the ICU however it takes a long time to set up and achieve appropriate conditions to perform. In addition, emergency recordings may be difficult to organize within the tight schedule of a hospital EEG unit.

Because the usual means for predicting outcome have limitations, simple clinical means of assessment are still warranted. During acute brain hypoxia the patient does not respond to painful stimuli. Brain stem reflexes consisting of occulocephalic and occulovestibular (caloric) responses, corneal reflexes and pupillary light reflexes are absent. Motor responses including defensive posturing and withdrawal, also are absent while muscle stretch reflexes are depressed. Recovery from this level of function is possible only if there is prompt restitution of brain perfusion and adequate oxygenation of the brain cells (*12*).

When recovery occurs it begins with the return of brain stem reflexes followed by progressive restitution of more rostral functions. Fundamental observations regarding light reflexes, eye movements, motor responses and responses to commands that are invaluable in helping to predict outcome after hypoxic brain injury are presented in table 1.

Table 1: Post-cardiac Arrest and Recovery of Function: Significant clinical signs

	Worst Prognosis	Best prognosis
Initial exam	No pupillary light reflexes	Pupillary light reflexes present Eye movements roving, conjugate or orienting; motor responses flexor or extensor
1 day	Eye movements neither roving, conjugate or orienting; motor responses flexor	Eye opening improved; motor responses withdrawal or better
3 days	No spontaneous eye opening; motor response remains no better than flexor	Spontaneous eye movement normal; motor response withdrawal or better
1 week	Eye movements neither conjugate, roving nor orientating; motor responses as of day 3; does not obey commands	Obeys commands
2 weeks	Motor response as of day 3 persists; does not obey commands	Occulocephalic response normal

(Adapted from Clinical Neurology Vol. 2) (*12*)

Thus with clinical assessment one can predict prognosis but perhaps not the extent of brain damage and subsequent recovery. There is increasing awareness that, if the eventual outcome of patients in coma could be predicted accurately within hours of a cardiac arrest, resuscitative measures could be concentrated on patients for whom there was a reasonable chance of recovery (5).

CEREBRAL RESUSCITATION AND PROTECTION

Ischaemia reduces the brains supply of metabolic substrates such as O_2 and glucose. Abrupt cessation of cerebral blood flow results in a depletion of high energy phosphate stores within 2 minutes and then an isoelectric line on EEG (*41*).

The function and structural integrity of the brain is related closely to its blood supply (*5*). It therefore follows that, given an adequate supply of oxygenated blood, the brain will be protected from the adverse effects of hypoxia. However, most

patients with hypoxic brain damage are first seen only after the signs and symptoms of irreversible damage have already developed (*5*). The outcome after global arrest depends on the duration of ischaemia and the relationship between ischaemic cellular membrane failure and the subsequent development of irreversible damage (*39, 40*).

The idea of cerebral protection has since come into play with considerable research being undertaken to find ways to minimize hypoxic brain damage (HBD). Cerebral protection involves interventions instituted before the ischaemic insult with improved tolerance of the brain to that insult while cerebral resuscitation refers to intervention instituted after onset of ischaemic insult (*41*). There are two main ways to ameliorate HBD (*28*). First, by the overall inhibition of metabolic activity, in order to reduce the oxygen and substrate requirements of the brain. Second, by improving mitochondrial efficiency in order to optimize energy output in the presence of a reduced O_2 supply. Under hypoxemic conditions reactive oxygen species are formed (*82*) which have a detrimental effect on mitochondria with resultant respiratory chain dysfunction, increased permeability and cell death. This has led to research on the use of anti-anoxic drugs, which may improve mitochondrial efficiency (*5*).

A most efficient procedure for inhibition of metabolic activity is hypothermia. Hypothermia is defined as a core body temperature of less than 35^0C (*37*). It can be classified as mild (35-32^0C), moderate (<32-28^0C) and severe (<28^0C) (*43*).

Cerebral metabolic rate undergoes a log-linear reduction, as brain temperature is progressively reduced (42). Studies done on dogs have shown that mild cerebral hypothermia started during or immediately after external CPR improves neurological

recovery (*29*). The mechanism of neuroprotection from mild hypothermia seems to be not only a decrease in cerebral metabolism but also involves a specific action on some intracellular events such as the blocking of the release of glutamate and of lipid preoxidation in brain tissue. An indirect proof of the neuroprotective effect of moderate hypothermia is the increase in the neuronal damage induced by moderate hyperthermia (9).

Another approach to inhibit metabolic activity of the brain is the use of barbiturates and non-barbiturates anesthetics such as isoflurane and propofol (*30, 31*). Barbiturates reduce the cerebral metabolic rate by 50% (*41*). Administration of short-acting metabolic depressants drugs might be beneficial since they provide distinct depression of metabolism while increasing blood flow conditions (*38*).

However, it is conceivable that moderate hypothermia could exert a better neuroprotective effect than the drugs having this reputation (9).

Research has presented a paradox that even though the brain is wholly dependent on the continuous delivery of glucose for its energy requirements, it has been found that the ischaemic or hypoxic brain finds continued glucose availability detrimental (*41,45-49*). This is because glucose will provide the substrate necessary for continued anaerobic metabolism in the ischaemic brain resulting in worsening lactic acidosis, which exacerbates tissue damage (51). However, adequate nutritional support and at least normal glucose levels are required to supply needed metabolic substrates for tissue repair (*49, 56*).

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Some basic principles brain-oriented intensive care (*51*) for survivors of cardiac arrest are:

- Normotension throughout coma (e.g. mean arterial pressure 90-100mmHg or normal systolic pressures for patient): titrated fluids and vasoppressors as needed
- Moderate hyperventilation (arterial PCO_2 30-35mmHg)
- Moderate hyperoxia (arterial PO_2 >100mmHg): titrated FIO_2; least positive end-expiratory pressure (PEEP) possible
- Arterial pH 7.3-7.5
- Immobilization (neuromuscular paralysis) as needed
- Sedation (morphine, diazepam) as needed
- Anticonvulsant (e.g. Diazepam, phenytoin, barbiturates) as needed
- Normalization of blood chemistry (hematocrit, electrolytes, osmolality and glucose)
- Osmotherapy (mannitol or glycerol) as needed for monitored intracranial pressure elevation or secondary neurological deterioration
- Normothermia
- Nutritional support started by 48hrs

PERSISTENT VEGETATIVE STATE

Although there appears to be a reduction in mortality following cardiac arrest, there does unfortunately appear to be an increasing number of patients who survive in a vegetative state (*13, 23*). The term persistent vegetative state (PVS) was first

used by Jennet and Plum (1972) to describe a condition in patients with severe brain damage in whom coma had progressed to a state of "wakefulness without awareness" (*13*). The distinguishing feature of PVS is an irregular but cyclic state of circadian sleep and wake cycles, unaccompanied by any detectable expression of self-awareness. Along with maintaining autonomous functions such as cardiovascular and renal functions, the patients may be aroused by certain stimuli, opening their eyes if they were closed, changing their facial expressions, or even moving their limbs. They may grind their teeth, swallow, smile, shed tears, grunt, moan, or scream without any apparent reason. Consistent with PVS is a lack of sustained visual pursuit. Although they move their eyes, they neither fixate on a visual object nor track a moving target with their eye (*14*). Thus, although these patients may exhibit behavior that appears to be the result of conscious thought and reasoning, these behaviors are merely reflexive and do not indicate awareness (*14*).

The Multi-Society Task Force on PVS defines persistent vegetative state as a vegetative state present one month after acute traumatic or non-traumatic brain injuries. Recovery from a non-traumatic PVS after 3 months is exceedingly rare in both adults and children (*14*).

BRAIN DEATH

Fewer than 50 years ago a person who had stopped breathing and had no heart beat was considered dead. Now, however, brain function is also considered in the definition of death. Two French neurophysiologists' Mallaret and Guolon, who studied patients on artificial life support who showed no electrical brain activity,

introduced the actual concept of brain death in a 1959 article. They concluded that these patients were "beyond coma" (*15*). No definitive standard of brain death emerged until a group of physicians, theologians, lawyers and philosophers on the Harvard University faculty formed the Ad Hoc Committee of Harvard Medical School to examine the definition of Brain Death in early 1968 (*16*). According to the report, a permanently non-functioning brain must exhibit four criteria:

- Unreceptivity and unresponsivity, in which there is a "total unawareness of externally applied stimuli" (unresponsive coma)
- No movements (absence of postural activity such as decerebration) or spontaneous breathing during a period of at least 1hr in which the patient is continuously being observed by a physician
- Absence of brain stem and spinal reflexes: no reflexes such as blinking, eye movements and stretch-of-tendon reflexes
- A flat EEG (with correct electrode placement, functional equipment and competent operator).

Induced hypothermia and the presence of central nervous system depressants such as barbiturates must be excluded. In severe hypothermia (core temperature $<28^0$C) coma can be associated with an isoelectric EEG and therefore in these cases is not indicative of brain death, as it may be reversible (*43*). Finally, the clinical and EEG findings should be unchanged in a second evaluation at least 24 hours later.

The Harvard Criteria as these standards came to be known have proven to be reliable indicators of brain death and physicians have generally reached a consensus about their continual application.

THE ROLE OF ANCILLARY TEST IN THE DIAGNOSIS OF BRAIN DEATH

The diagnosis of brain death is mainly a clinical one, but from time to time a clinician may seek guidance from a variety of ancillary tests. The most common such test is the EEG from which the expected finding would be a " flat" or "isoelectric" EEG. Observing a flat auditory brain stem response (ABR) (17) can facilitate confirmation of brain-stem death. Four-vessel angiography and radionuclide studies can be used to demonstrate the absence of cerebral circulation (*18*). More recently, absent flow signals on Transcranial Doppler ultrasonography have also been suggested as a method to demonstrate the absence of cerebral circulation in brain death (*19, 20*).

All these methods suffer from potential technical problems that require skilled technical support to make the techniques useful and reliable in the ICU environment (*21*). As a result, other criteria have been developed that do not require these ancillary tests as a prerequisite to the diagnosis of brain death.

One such criterion is the "Minnesota Criteria", in which notably excluded are absent spinal reflexes and EEG (*21,33*). The key elements of the Minnesota Criteria are:

- Absence of spontaneous movement
- Absence of spontaneous respiration over a four minute test period

- Absence of brain stem reflexes as evidenced by fixed dilated pupils, absent gag, corneal and ciliospinal reflexes, absent doll's eye movements, absent responses to caloric stimulation and absent tonic neck reflex
- Unchanged clinical status for at least 12 hours; and
- Responsible pathological process deemed irreparable (*33*).

SPECIAL CIRCUMSTANCES: NEONATES AND YOUNG CHILDREN

In children with a conceptual age of 52 weeks or older (more than 2 months post-term) the adult clinical criteria of brain death can be applied. Clinical criteria alone are not sufficient in the determination of brain death in infants under this age (*34, 35, 36*).

The basic tenets accepted in adults that apply to children include:

- The importance of excluding remediable or reversible conditions, special toxic and metabolic derangement and the effects of sedative drugs, paralytic agents, hypothermia and hypotension
- Physical examination criteria must be satisfied
- Irreversibility must be ensured by re- evaluation at specified intervals

It is recommended that for a term neonate (greater than 38 weeks gestation) and young infants aged 7 days to 2 months, the clinical examination and a radionuclide brain flow is done. For those 2 months to 1 year, two examinations and EEG's separated by at least 24 hours is suggested. Lastly, for those over 1 year of age an observation of at least 24 hours is recommended following hypoxic brain injury before a diagnosis of brain death can be made (*34*).

A brain death diagnosis criterion in children (60) is summarized as follows:

I. Prerequisites

- Irreversible lesion/ event
- Known etiology of lesion/event
- Hemodynamically stable and normothermic during observation
- No drugs of sedation or neuromuscular blockade at time of examination

II. Physical examination

- Coma; no response to sound, light or deep pain (Glasgow Coma Scale <8)
- No spontaneous movement or posturing and or flaccid tone
- Absent brain stem reflexes- pupillary light reflex, corneal, occulocephalic, occulovestibular, oropharyngeal (gag) reflexes; facial grimace with nasopharyngeal stimulus gag
- Apnea

III. Period of observation

- No definite consensus; period ranges from 6-48hrs; is specific to age group

IV. Corroboratory test

- Cerebral angiography
- EEG
- Radioisotope cerebral blood flow study
- Transcranial Doppler ultrasonography

RESUSCITOLOGY

Resuscitology refers to resuscitation research, the main target of which is "brains too good to die" (*68*), a concept that was introduced in the 1970's and forms the basis of the changing face of cardiopulmonary cerebral resuscitation (CPCR). Brain resuscitation research programs have concerned themselves with reversing the effects of global ischaemic anoxia following cardiac arrest. As a result resuscitation has expanded beyond the phase of emergency resuscitation to include long-term resuscitation, which is also known as prolonged life support (*61,66*), for the support of multiple organs (*67*) and for brain resuscitation (*61,79, 80*). Prolonged life support is post-resuscitative intensive care and consists of determining and treating the cause of death while assessing the patient's salvageability, optimizing human mentation by brain -specific resuscitation measures and lastly intensive care.

Resuscitology is of socioeconomic importance because about one-half to three-quarters of survivors of CPR attempts die early after cardiac arrest from multiple organ failure, primary cardiac failure or postanoxic brain death (*69*). In addition, it has also been found that of the long-term CPR survivors, 10-30% suffer costly permanent brain damage (*23, 70-74*).

Critical care and resuscitation is at the core of an anesthesiologist training in this country placing on them the need to be informed of recent advances which will enable them to provide adequate and appropriate brain-oriented intensive care. The medical importance of resuscitology (61) includes:

1) the need for effective therapies

2) development of more reliable measurements of outcome prediction to recognize and stop futile therapy
3) the fact that more effective treatment for restoring brain function after cardiac arrest might lead the way to more effective management of other types of brain insults.

Growth in technology and our ability to more successfully resuscitate and maintain life has resulted in more patients surviving with significant brain damage including persistent vegetative states (*13, 23*). This has presented new dilemmas in ethical issues (bioethics). Objective analysis of these issues requires factual data, clarity, and examination of motives and consequences in addition to application of established rules, principles and customs (*82*). Thus, there is a need for all critical care specialists to be involved in resuscitology.

OBJECTIVES

OVERALL OBJECTIVE

To describe the phenomenon of Hypoxic Brain Damage (HBD) in patients admitted into the Kenyatta National Hospital Intensive Care Unit (KNH ICU).

SPECIFIC OBJECTIVES

1. Evaluate the criteria for diagnosis of HBD at KNH.
2. Determine the common etiological factors associated with HBD at KNH.
3. Observe the assessment, management and eventual outcome of patients with HBD.
4. Generate hypotheses about possible cause and effect associations between variables that may form the basis for further studies on HBD as it occurs in KNH.
5. Make recommendations on the possible way forward in the prevention of HBD.
6. Make recommendations on the management of patients admitted to the KNH ICU with HBD.

RATIONALE

Hypoxic Brain Damage (HBD) is a condition recognized to be associated with high morbidity and mortality. A significant number of affected individuals have to be admitted into an Intensive Care Unit.

Diminished O_2 supply to the brain may produce profound cognitive, physical and affective impairments which may be slow to recover, or may never recover. The ultimate degree of neurological recovery after hypoxic brain injury may range from brain death and the vegetative state, to minor psychiatric disturbances and even apparent normality. In severe cases, hypoxic-anoxic brain injury can have a catastrophic impact in terms of functional deficits as well as on the costs involved in treatment. Patients who have suffered significant brain damage require rehabilitation that may be long term, resulting in depletion of the family's financial and emotional resources. It thus contributes to considerable instability and disruption within families.

The severity of the initial insult and whether or not adequate resuscitation was commenced before brain damage becomes irreversible determines the extent of neurological recovery. Minimizing response times and optimizing cardiopulmonary resuscitation (CPR) performance improves outcome for patients. With the advent of basic and advanced cardiac life support, all medical personnel are required to have skills to administer CPR. A significant number of medical and paramedical personnel in Kenyatta National Hospital have undergone training on how to administer basic and/or advanced life support.

In recent times, it has become clear worldwide that an emphasis must be placed not only on cardiopulmonary resuscitation, but also just as importantly on cerebral resuscitation. It is recognized that hypoxic damage to the brain will occur following cardiac arrest, respiratory failure or any other condition that leads to decreased cerebral blood flow. This study will look at the most common factors in the etiology of HBD and will form a basis for the modification of cardiopulmonary cerebral resuscitation (CPCR) at Kenyatta National Hospital with regard to reducing HBD following resuscitation. A thorough review of previous studies revealed no prior research had been undertaken in Kenyatta National Hospital (KNH) on this condition. The findings of this study will also form a basis for further research on methods to protect the brain from hypoxic-ischaemic injury, as well as ways to improve the neurological outcome of patients who may sustain hypoxic insult to the brain.

Finally, this study will form a useful database in the generation of criteria for diagnosis and management of HBD.

METHODOLOGY

STUDY SITE

The study was conducted in KNH-ICU and HDU. Both the ICU and HDU formed the study site since the HDU many times doubles up as an ICU, if the ICU is congested.

STUDY POPULATION

Data was collected on all patients who were admitted into the ICU and HDU during the period of 1st January 1995 to 31st December1999 with the diagnosis of HBD.

Inclusion Criteria

- All ages
- Both male and females
- Had not been admitted to the any ICU or HDU previously

Exclusion Criteria

- Patients with head trauma
- Patients with brain damage previous to the hypoxic incident

STUDY DESIGN

Retrospective, descriptive, cross-sectional survey.

STUDY PERIOD

Five-year period from 1st January 1995 to 31st December1999.

SAMPLE SIZE

The number of patients who were admitted to the ICU and HDU with HBD over the stipulated study period determined the sample size. Purposive sampling

methods were used. This is a deliberately non-random method of sampling, which aims to sample a group of people with a particular characteristic. In this case, all patients with HBD were used.

DATA MANAGEMENT

A list of patients admitted to the ICU and HDU with a diagnosis of HBD was obtained from the admissions book in the ICU and HDU. The files of the patients were then retrieved from the Records Department at KNH.

Data was extracted from files of all the patients admitted into the ICU and HDU over the above study period. The information was then collected using a data collection form (see appendix 1) and centered on:

- Sociodemographic Characteristics
- Diagnosis on admission
- Source of the patient
- Events preceding admission, focusing mainly on any resuscitation done
- Clinical assessment of the patient during their stay in the ICU and HDU
- Management of the patient, including any investigations done
- Outcome

The results of this study were analyzed and have been presented in the form of tables, pie charts and bar graphs. A detailed discussion follows on the phenomenon of HBD at KNH. Appropriate conclusions and recommendations are documented in the form of a thesis and submitted to the Supervisor of this project and other subsequent examiners. Copies of the thesis with the findings have been made

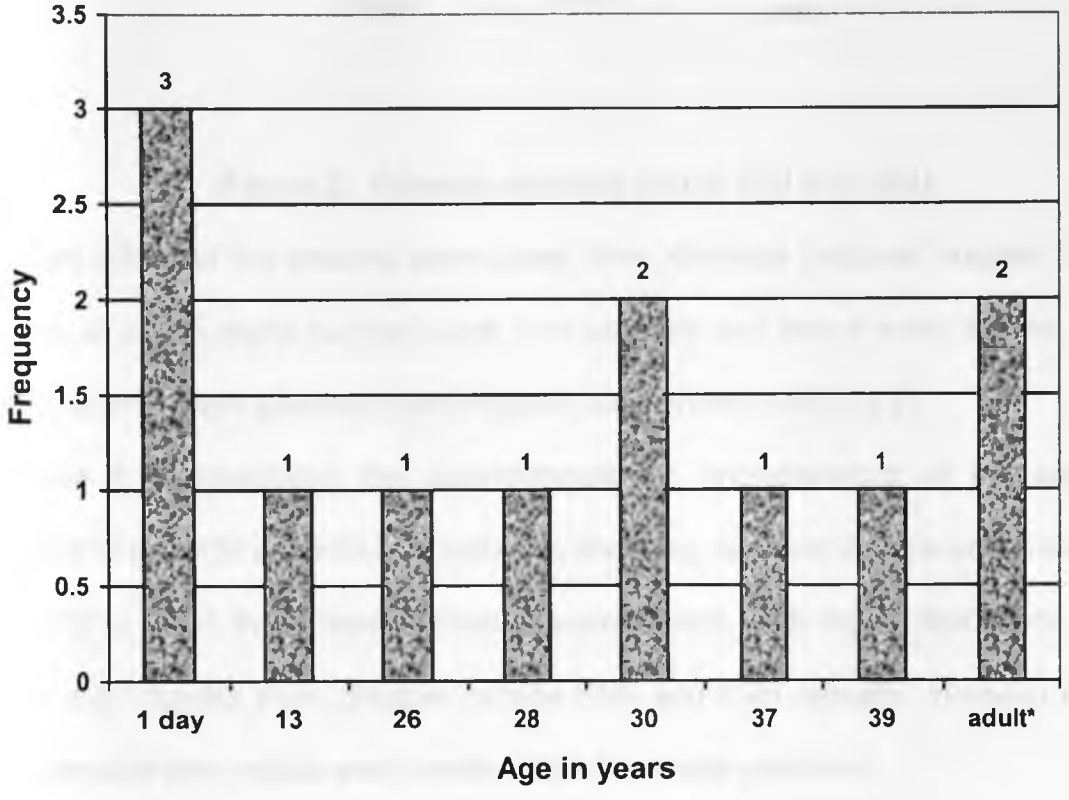
available to the University of Nairobi Library for public consumption, adding to the database of knowledge on the subject of Hypoxic Brain Damage.

ETHICAL CONSIDERATIONS

- All information obtained from this study was handled with absolute confidentiality and was used only for the intended purposes.
- Since this was a retrospective study, a consideration of harm to patients was not relevant.
- The protocol was submitted for approval to the ethical committee at Kenyatta National Hospital before the research is undertaken.

RESULTS

Data was retrieved from a total of twelve patients admitted to the KNH ICU and HDU from 1st January 1995 to 31st December 1999 and included all age groups of patients admitted with a diagnosis of Hypoxic Brain Damage (HBD). The results are summarized with the use of tables and figures in the following section.



adult*- undefined age

Figure 1: Age distribution

Three (25%) of the patients were neonates while the remaining nine (75%) were adults of varying ages from 13-39yrs (fig 1). Two adults did not have their ages indicated.

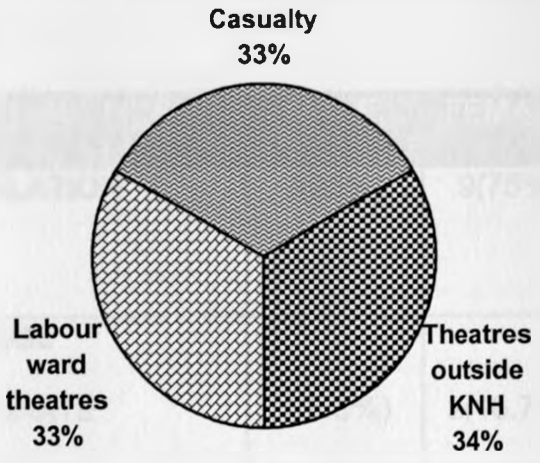


Figure 2: Primary referring unit to ICU and HDU

Eight (66%) of the patients were drawn from Kenyatta National Hospital (KNH) directly, of which equal number were from casualty and labour ward theatre. Four (34%) patients were admitted from hospitals surrounding KNH (fig 2).

Table 2 demonstrates the sociodemographic characteristics of the patients admitted to the ICU and HDU according to their sex, age and source on admission. Nine (75%) of all the patients admitted were female, with equal distribution from labour ward theatre KNH, theatres outside KNH and KNH casualty. However of the three females from labour ward theatre KNH, two were newborns.

The three (25%) males were admitted from as follows, one (8.3%) was from labour ward theatre KNH, a neonate, one (8.3%) from theatres outside of KNH and one (8.3%) from KNH Casualty (table 2).

TABLE 2: Sociodemographic characteristics of patients admitted to KNH ICU and HDU with HBD.

CHARACTERISTICS	MALE	FEMALE
POPULATION	3(25%)	9(75%)
AGE		
NEONATE	1(8.3%)	2(16.7%)
ADULT	2(16.7%)	7(68.3%)
SOURCE		
CASUALTY	1(8.3%)	3(25%)
LABOUR WARD KNH*	1(8.3%)	3(25%)
THEATRES OUTSIDE KNH*	1(8.3%)	3(25%)

*Kenyatta National Hospital

The duration of stay within the ICU and HDU varied from 1-9 days (fig 3) with the average stay being three days.

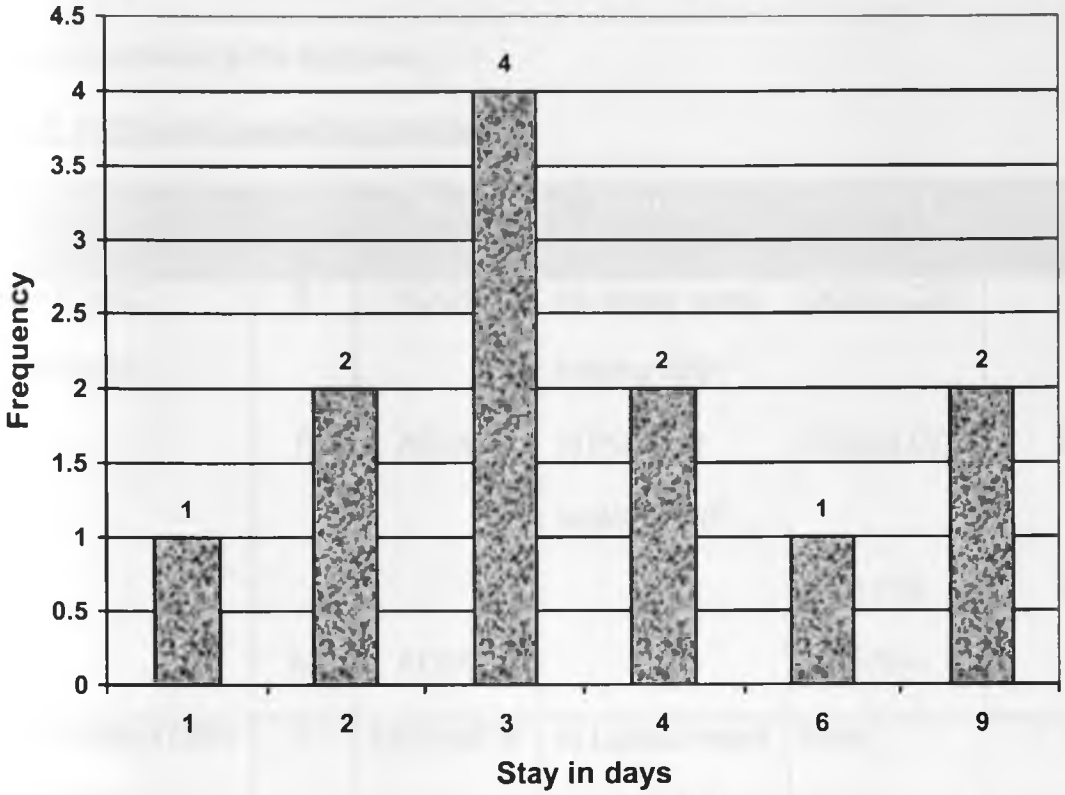


Figure 3: Duration of stay within ICU and HDU

The causes of resuscitation were cardiac arrest, in five (43.3%) patients, and respiratory arrest in the remaining seven (56.7%) (table 3). In only one (8.3%) was the duration of cardiac arrest recorded and this was 5 minutes.

The five (43.3%) patients who had cardiac arrest were from theatre. One (8.3%) patient had cardiac arrest at induction of anesthesia, two (16.7%) intraoperatively and two (16.7%) postoperatively. The reason for the cardiac arrest was not indicated, except for the one patient who had cardiac arrest at induction, which was due to a difficult airway necessitating an emergency tracheostomy.

The reason for respiratory failure was only indicated in two patients (neonates) and was due to severe birth asphyxia.

TABLE 3: Events preceding admission

INSULT	SEX	AGE	SOURCE	EVENT	NUMBER
CARDIAC ARREST	F	ADULT	a)Labour ward theatre KNH*	During C/S[1]	1
	F	ADULT	b)Theatres outside KNH	During C/S	2
				Post C/S	1
	M	ADULT		Induction	1
RESPIRATORY ARREST/ FAILURE	F	NEONATE	a) Labour ward theatre KNH	Birth Asphyxia	2
	M	NEONATE	"	"	1
	F	ADULT	b) Casualty	Unknown	3
	M	"	"	"	1

*Kenyatta National Hospital

C/S[1] Caesarian Section

All twelve patients were ventilated during and post resuscitation either via an endotracheal tube, eleven (91.7%); or tracheostomy, one (8.3%) patient.

The vital signs (blood pressure, heart rate and temperature) on admission to the ICU and HDU are summarized in table 4 below and a row is added at the bottom to indicate the number of patients on CNS depressants.

TABLE 4: Summary of patients admitted with normal and abnormal vital signs (see appendix 3 for normal values)

VITAL SIGNS	YES	NO	UNKNOWN
Hypotension	3(25%)	6(50%)	3(25%)
Bradycardia	1(8.3%)	11(91.7%)	0
Hypothermia[1]	6(50%)	5(41.7%)	1(8.3%)
CNS* Depressants	3(25%)	9(75%)	0

*Central nervous system

[1] Skin temperature 32-35^{0}C. No core temperature available

All three (25%) patients who were hypotensive had associated hypothermia (skin temperature 32-35^{0}C). Of the three (25%) patients whose blood pressure was unknown, two were neonates. The one (8.3%) patient who was bradycardic was not hypotensive or hypothermic.

The central nervous system depressants the three (25%) patients had been given were, Diazepam (one patient), Phenytoin (one patient), both given for the control of convulsion before the patient was admitted. Tramadol and Midazolam were given to one patient intraoperatively as part of the anesthetic used.

Various investigations were done on the patients on admission to the ICU and HDU and included arterial blood gases, random blood glucose, serum sodium and potassium.

Seven (58.3%) of the patients had acidosis (pH <7.35), three (25%) respiratory and four (33.3%) metabolic in origin. One patient (8.3%) had a respiratory alkalosis

(pH >7.45). Only three patients (25%) were found to have normal blood pH. In one patient no pH results were recorded.

Six (50%) of the patients had hypoxaemia (PO_2 <10 kPa), however only two (16.7%) had saturation pressures of oxygen (SaO_2) of <90%. Two (16.7%) had SaO_2 of 90-95% and seven (68.3%) had SaO_2 of >95%.

TABLE 5: Summary of Blood glucose, sodium (Na^+) and potassium (K^+) levels.

	Below	Normal	Above	Unknown
Blood glucose	1(8.3%)	2(16.7%)	8(66.7%)	1(8.3%)
Na^+	9(75%)	1(8.3%)	0	2(16.7%)
K^+	7(58.4%)	3(25%)	1(8.3%)	1(8.3%)

Majority of the patients had abnormal blood glucose and electrolyte levels on admission. Seven (58.4%) patients were hypokalemic, nine (75%) were hyponatremic and eight (66.7%) were hyperglycaemic (table 5).

Neurological examination comprising of corticular, brain stem and motor function was extracted from the files of all twelve patients. Corticular function includes Glasgow Coma Scale (GCS), memory, orientation, vision and speech; however, only the GCS was assessed on the patients. On the day of admission, ten (83.3%) had a GCS of 3/15, one (8.3%) had a GCS of 4/15 and one (8.3%) was not assessed because the patient was paralyzed and sedated on admission (table 6). All three neonates had a modified peadiatric score of 3/15 on admission.

TABLE 6: Glasgow Coma Scale (GCS) and Pupillary reaction findings in patients with HBD at admission, 24hrs, 48hrs and one week.

	OA*	24HRS	48HRS	1 WEEK
NEONATES	3	2	2	0
GCS				
3/15	3	2	2	0
Pupillary response				
Reacting to light	0	0	0	0
No reaction to light				
1. Mid-dilated	3	1	1	0
2. Fully dilated	0	1	1	0
ADULTS	9	9	7	2
GCS				
3/15	7	7	5	1
4/15	1	0	0	0
6/15	0	1	1	0
Not done	1	1	1	1
Pupillary response				
Reacting to light	3	2	2	0
No reaction to light				
1. Mid-dilated	2	2	1	0
2. Fully dilated	4	5	4	2

* on admission

All the patients who had a GCS of 3/15 at admission remained with the same GCS through out their stay in ICU and HDU. The patient who had a GCS of 4/15 on admission had improved to a GCS of 6/15 over the preceding 24-48hours however by the end of one week the GCS had deteriorated to 3/15 (table 6). The one patient who was paralyzed and sedated did not have GCS done through out the nine days the patient was admitted into ICU/HDU.

In the assessment of brain stem function, only pupillary light reflex was performed on all the patients throughout their stay. The neonates had pupils that were mid-dilated and not responsive to light on the first day of admission. After 24hours, one neonate died and of the two remaining, one had persistently mid-dilated non-responsive pupils while the other neonate had fully dilated and fixed pupils until their death 24hours later.

In the adult age group, three out of nine patients (33%) had pupils that were responsive to light on admission however after 24hours, only two still had responsive pupils. Of the remaining adults, four (44.4%) had dilated and fixed pupils on admission while two (22.2%) had mid-dilated non-responsive pupils. After 24hours, five patients had dilated and fixed pupils. At 48hours, two adult patients had died and of the remaining seven, four had fixed and dilated pupils, two had reactive pupils, one had mid-dilated non-responsive pupils while one was not indicated.

Occular movements and corneal reflexes were not recorded on any of the patients. Respiratory patterns of breathing documented on two patients; one as gasping and the other as normal. One patient had gag reflex documented as absent.

Of the eleven patients who were not paralyzed and sedated, only two (16.7%) had motor function assessments done. However even for the latter two, assessment was incomplete as only the tone was indicated. Both were hypotonic.

In the management of patients, all twelve (100%) patients received antibiotics throughout their stay in ICU and HDU. Eleven (91.7%) were artificially ventilated. The one (8.3%) who was not ventilated had a tracheostomy and a good respiratory effort. Three (25%) of the patients admitted had hypotension however only one (8.3%), was given ionotropic support. Four (33.3%) patients were put on steroids (dexamethasone) as part of their management.

On the clinical outcome of the patients, eleven (91.7%) died and one was transferred out of the unit alive but with a tracheostomy. By 72hours, 50% (6 patients) of all the patients admitted with hypoxic brain damage had died. The longest stay was nine days (2 patients).

Only four (33.3%) of the patients admitted with HBD were assessed for brain death, all of who were adult patients. Two of the patients were assessed 24 hours after admission; one after 72hours and one after seven days. A Senior House Officer, a post-graduate student in anesthesiology, did the brain death assessments.

DISCUSSION

Less than 10% of all CPR attempts pre-hospital or in hospital outside special care units result in survival without brain damage (*8*). Over the past five or so years, a significant number of medical personnel in Kenya have undergone training in basic and advanced life support techniques of CPR with an aim of improving the quality of health care. As a result many lives have been salvaged. A study done in KNH-ICU by Ikamba (32) showed that cerebral anoxia contributed 10% to the development of brain death within the ICU. No local study is available to show how many CPR attempts either within or outside KNH result in survival with brain damage. From this study, however, it can be appreciated from the data analyzed that the patients had severe hypoxic brain damage indicated by a GCS< 8. However due to the small sample size and the fact that of the twenty-five patients admitted with HBD, only twelve files were retrievable from the records department, this data may not be a true reflection of the range of neurological deficits that may have occurred post-CPR during that period.

Patients' outcome in terms of survival and overall performance capability (human mentation) depends on the severity and duration of the insult (*66*). This being a retrospective study, one does not have the benefit of being able to interview the health personnel involved in the resuscitation to elicit more information on the duration and severity of insult that necessitated resuscitation and therefore this information was inadequate. However it may be suggested that the anoxic period may have been long since anyway an accurately timed anoxic period is likely to be

brief as immediate resuscitative action is taken and therefore these patients do not pose a prognostic problem (*12*).

In a previous study (*2*) undertaken elsewhere, cardiac arrest was noted to be the most common cause of HBD. This study done at KNH reflects an almost equal contribution from respiratory arrest (58%) and cardiac arrest (42%). Due to the previously cited limitations of this study, it is only possible to document the important etiological factors but not to accurately quantify eachs' contribution to the development of HBD at KNH. In a study by Groswaser (*10*), cardiac arrest following anaesthetic accidents contributed 32% to the incidence of HBD. Cardiac arrest was attributable in 41% of the cases of HBD at KNH and they all occurred in the peri-operative period. Although this study may show that anesthetic related accidents contributed immensely to the development of HBD, it must be noted that this could be due to that fact that patients are monitored in the peri-operative period therefore any cardiac arrest would be noticed and resuscitation commenced. Despite this though, the patients still had significant brain damage post-resuscitation.

Minimizing response times and optimizing CPR performance would certainly improve these results (*8*) as patients' outcome also depends on the speed and quality of emergency resuscitation (*66*). Post-CPR intensive therapy must be started immediately and be of high quality for it to influence neurological recovery. Cardiopulmonary, hepatic and renal function must be monitored and optimized to support survival and recovery of cerebral function (*66*). All patients who have undergone resuscitation should be admitted into an ICU setting so that the reason for clinical deterioration can be better ascertained. Depending on the clinical status

of the patient, appropriate long-term resuscitative measures should then be instituted with reason.

The patients admitted to the ICU/HDU were ventilated post-CPR with only one patient being paralyzed (curarized) and sedated. Despite this however, 50% of the patients had a PaO_2 of 10kPa (75mmHg) on admission. Brain-oriented intensive care begins with stabilization of the cardiopulmonary system. Management post-CPR should enhance adequate tissue oxygenation to preserve cellular function and to allow post-ischaemic reparative processes to occur (51). In a comatosed patient, ventilation should be stabilized using mechanical ventilation and paralysis (if necessary), maintaining the PaO_2 at above 100mmHg with an FIO_2 of 90-100% in the first one to six hours post-CPR (66). The FIO_2 can then be tapered down to the lowest possible level to maintain a PaO_2 of atleast 90mmHg, with the use of PEEP if necessary (*51, 66*). This prevents transient pulmonary problems from causing a significant deterioration in already compromised tissues. Ventilation should be continued till the patient regains consciousness or is able to maintain adequate respirations on his or her own. Mechanical ventilation with partial neuromuscular blockade allows for prolonged immobilization, which facilitates control of blood pressure and arterial blood gases thereby reducing to severity of brain damage.

Seven (58.3%) of the patients had acidosis (pH 7.35), in which three were respiratory in origin. Acidosis causes central nervous system depression and limits cell survival (*52, 55*). Hyperventilation is important in the management of respiratory acidosis and may correct post- ischaemic tissue acidosis. Experimental data strongly

(*55*) suggests that therapeutic measures aimed at preventing or ameliorating tissue acidosis are of significant clinical benefit in limiting HBD.

Cardiovascular homeostasis involves maintenance of normotension (MAP 90mmHg or SBP 120-130mmHg or normal for patient), ECG monitoring with prevention and control of dysrythmias (*66*). Three (25%) patients had SBP <90mmHg (of which only one had ionotropic support) while one (8.3%) had bradycardia (heart rate< 50 beats/min). Maintenance of adequate cerebral perfusion is the main stay of treatment. Arterial pressure should be rapidly normalized in patients having hypotension by using carefully calibrated fluids and vasopressors (*84*) as hypotension can cause severe compromise of cerebral blood flow and result in significant additional brain damage (*53*). In the normal brain, autoregulation compensates to an extent for hypoperfusion (44). During ischaemia, accumulation of tissue metabolites and abnormal calcium influxes cause autoregulation to be compromised (false autoregulation) if not lost (52). Perfusion of the ischaemic brain then becomes dependent on arterial pressure. Some authorities (*66*) imply that brief mild hypertension (MAP 120-140mmHg) may be desirable after restoration of spontaneous circulation following CPR (automatic owing to the epinephrine used during CPR). It is can therefore be seen that hypotension and dysrythmias of all sorts should be treated aggressively to prevent secondary brain damage.

In addition to cardiopulmonary, renal and hepatic support, brain-orientated intensive care involves maintenance of optimal hematocrit, electrolytes, blood glucose and alimentation (66). Of the patients admitted with HBD, eight (66.7%) had hyperglycaemia, one (8.3%) hypoglycaemia, six (50%) hyponatremia and seven

(58.3%) hypokalemia. All of these electrolyte abnormalities could have contributed to the development of cardiorespiratory arrest pre-admission but also to worsening of neurological function (*45-50, 56*) with resultant high morbidity and mortality. It must be emphasized that survival of the brain and indeed the whole being is dependant on optimization of the cardioresipratory, hepatic and renal systems and but also the normalization of metabolic status. These measures must be instituted immediately after resuscitation for them to positively influence recovery.

Other brain-oriented treatments include temperature control, anticonvulsant therapy and corticosteroids (51). Shivering, restlessness and seizure activity increase oxygen consumption two- to threefold (*66*). Patients should be kept normthermic in the post-ischaemic period unless hypothermia is induced as a specific brain resuscitation measure (*9, 29, 42*). Steroid therapy is optional and shows no additional benefit (*57, 66, 78*). None of the newer methods of cerebral protection (induced hypothermia, barbiturate and anesthetics therapy) that are under investigation in other countries were used on any of these patients. It still remains to be seen whether they may be of benefit in our set up.

An important and difficult aspect of prolonged life support is the assessment of patient salvageability post-resuscitation. Early prediction of outcome to pursue therapy aggressively in the potentially salvageable patient or to limit therapy in the patient with no realistic hope of recovery is difficult and as yet not a science. Useful information can however be derived from simple neurological signs (*12,85*). With neurological assessment one may be able to predict outcome and thus be able to discuss with the relatives the likely prognosis. The worst prognosis is seen in

patients who have no pupillary response to light on the initial examination. However it must be noted that in the acute phase of HBD brain stem reflexes including pupillary light reflexes may be absent but this improves on prompt restitution of cerebral perfusion and adequate oxygenation (*12*). Seventy-five percent of the patients had unresponsive pupils on initial examination and on repeated examinations showed no improvement while the patients were in ICU. In addition all the patients had GCS of less than 8 indicating severe brain damage. This correlates with the high mortality and morbidity seen in these patients. Neurological examinations should be done frequently to enable recognition of awakening and focal lesions therefore fully paralyzing doses of neuromuscular blocking agent should be avoided. These examinations must also be complete so as to optimize treatment. In this study, it must be noted that neurological examinations were incomplete as only GCS and pupillary light reflexes were done on majority of the patients.

A patient who remains in unresponsive coma for more than 24 hours after optimization of treatment needs to have a brain death assessment done. This must be done in the presence of two physicians and repeated again after an appropriate interval. In neonates this interval is 48 hours while in adults it may be as short as six hours (*14*). Brain death assessments were only done in four patients (25%). None of these patients had CTScan done. A CTScan is imperative in ruling out a reversible cause of the brain damage, which is one of the prerequisites of brain death assessements (*33, 60*).

It is evident from this study that HBD carries a very high morbidity and mortality with 91% of the patients admitted dying within one to nine days. Only one patient was noted to have slight neurological improvement, GCS improving from 4/15 on admission to 6/15 after twenty-four hours in the ICU. However the patients' condition later deteriorated resulting in death nine days later. This perhaps emphasizes the need for the medical fraternity at KNH to participate in finding and optimizing treatment options that reduced hypoxic brain damage and to apply these treatments with reason. Since anesthesiologists are in the forefront of critical care, the onus is on them to lead the way in resuscitology.

The cost of care within the ICU/HDU is high and with the introduction of cost sharing, this financial burden is then transferred to the relatives who many times may not afford. It is thus necessary to have criteria for diagnosis and management of patients with severe HBD from which there is no hope of recovery. Perhaps the time has come for healthcare providers in KNH to aggressively tackle the ethical issues surrounding brain death assessment and its implication to patient care. All withstanding, it must be re-emphasized that prompt normalization of patients cardiopulmonary, renal, hepatic and metabolic systems is the mainstay of treatment of hypoxic-ischaemic brain injury in order to provide optimal conditions for recovery. This must occur before one can justify making a diagnosis of brain death within KNH-ICU and HDU.

CONCLUSIONS

1. All the patients admitted with Hypoxic Brain Damage had severe permanent brain damage.
2. Brain resuscitation is an important aspect of any successful cardiopulmonary resuscitation.
3. The most frequent cause of Hypoxic Brain damage at Kenyatta National Hospital was noted to be Respiratory failure and or arrest.
4. Cardiac arrest contributes significantly to Hypoxic Brain Damage resulting from perioperative accidents.
5. Hypoxic Brain Damage at KNH ICU and HDU is associated with a high mortality and morbidity.
6. HBD per se, may have contributed significantly less to the high morbidity and mortality associated with it in our set up if normalization of the patients' vital signs and electrolytes was done aggressively after resuscitation.
7. Mortality and morbidity is the same regardless of the age or patient source. Most patients were dying within 72hrs.
8. Diagnosis of HBD was made on the fact that a patient has neurological deficit after resuscitation. No methods of exclusion of other brain pathologies were used.

RECOMMENDATIONS

I. Emphasis needs to be placed on cerebral resuscitation, which forms an important aspect of basic, advanced and prolonged life support of Cardiopulmonary Resuscitation in KNH. This will reduce the morbidity and mortality of Hypoxic Brain Damage.

II. Proper documentation of resuscitation of patients should be made as accurately as possible.

III. Clinicians must be encouraged to thoroughly examine and diligently document all clinical findings of patients admitted to ICU/HDU with HBD. A checklist may be useful to meet this end.

IV. All patients admitted with HBD must have their vital signs and blood electrolytes and glucose normalized soon after resuscitation and admission to prevent further brain injury, which worsens the prognosis.

V. A protocol on Brain Death diagnosis in KNH needs to be made so that appropriate management of patients admitted to the ICU/HDU with HBD can be instituted early to maximize on the use of resources.

VI. Record keeping has to be made more efficient to prevent loss thus preventing review and research of relevant data. Computerization of all patient information would be of added advantage.

VII. A prospective study would need to be done to further characterize Hypoxic Brain Damage at Kenyatta National Hospital taking into consideration the new methods of cerebral protection.

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APPENDIX 1

DATA COLLECTION FORM

1. PATIENT CODE: _____ 2. AGE: _____ yrs_____months

3. SEX: _____

4. DIAGNOSIS ON ADMISSION:

_____

5. TOTAL STAY IN UNIT: _____ days

6. SOURCE: _____

EVENTS PRECEDING ADMISSION: (circle as appropriate)

- 7. CARDIAC ARREST YES NO DURATION _____
- 8. RESUSCITATION YES NO DURATION _____

If resuscitated,how_____

_____

ON ADMISSION:

WAS THE PATIENT

- 10. HYPOTENSIVE? YES NO
- 11. BRADYCARDIC? YES NO
- 12. HYPOTHERMIC? YES NO

13. ON ANY CNS DEPRESSANTS YES NO

IF YES, WHICH?

- NARCOTICS
- HYPNOTICS
- TRANQUILIZERS

❑ OTHER _____(specify)

INVESTIGATIONS ON ADMISSION

14. ARTERIAL BLOOD GAS: pH____ pO_2: ____kPa pCO_2: ____kPa

HCO_3 : _____ BE: _____ SPO_2 _____

15. Hb: _____g/dL 15. RBS: _____mmol/L 16.Na^+: ____meq/L

17.K^+ :_____meq/L

CTScan findings

_____

MANAGEMENT

ANTIBIOTICS YES NO DURATION _____

VENTILATION YES NO DURATION _____

If yes, reason_____

INOTROPIC SUPPORT YES NO DURATION _____

STERIODS YES NO DURATION _____

NEUROLOGICAL TESTING

	OA[1]	24HRS	48HRS	WEEK1	WEEK2
CORTICULAR FUNCTION					
GCS					
MEMORY					
ORIENTATION					
VISION					
SPEECH					
BRAIN-STEM FUNCTION					

PUPILLARY REACTION

OCCULAR MOVEMENTS

CORNEAL REFLEXES

RESPIRATORY PATTERN

GAG REFLEX

MOTOR FUNCTION

TYPE OF MOVEMENT

POSTURE

TONE

PLANTAR RESPONSES

TENDON REFLEXES

(OA^1- on admission)

OUTCOME (State in detail)

_____

_____

ANY DIAGNOSIS OF BRAIN DEATH? YES NO

If yes,

How soon after admission? _____ Days

By whom _____

APPENDIX 2

GLASGOW COMA SCALE		MODIFIED COMA SCALE FOR INFANTS	
ACTIVITY	BEST RESPONSE	ACTIVITY	BEST RESPONSE
EYE OPENING			
Spontaneous	4	Spontaneous	4
To speech	3	To speech	3
To pain	2	To pain	2
None	1	None	1
VERBAL			
Oriented	5	Coos, babbles	5
Confused	4	Irritable	4
Inappropriate words	3	Cries to pain	3
Nonspecific sounds	2	Moans to pain	2
None	1	None	1
MOTOR			
Follows commands	6	Normal spontaneous movement	6
Localizes pain	5	Withdraws to touch	5
Withdraws to pain	4	Withdraws to pain	4
Abnormal flexion	3	Abnormal flexion	3
Abnormal extension	2	Abnormal extension	2
None	1	None	1

From Jennet (58) and James (59)

APPENDIX 3

Reference Values (from KNH ICU lab)

Arterial Blood Gases

pH	7.35-7.45	
PCO_2	35-45mmHg	
PO_2	adults	80-90mmHg
	>65yrs	75-86mmHg
	newborns	60-70mmHg
SPO_2	96-99%	
HCO_3	22-26mmol/l	

Conversion factors:

mmhg= kPa x 7.5

kPa= mmHg x0.1333

Electrolytes

Na+	135-145mmol/l
K+	3.5-5.4mmol/l

Random Blood Glucose

RBS	2.5-6.8mmol/l

Tel: 726300 - 19
726550 - 9
726562 - 6
726450 - 9
726581 - 2
Fax: 725272

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NAIROBI.

Email: *knh@healthnet.or.ke*

Ref: KNH-ERC/01/1079

2 July 2001

Dr. Wagaki Wanguru
Dept. of Surgery (Anaesthesia)
Faculty of Medicine
University of Nairobi

Dear Dr. Wanguru,

RE: **RESEARCH PROPOSAL** "THE PHENOMENON OF HYPOXIC BRAIN DAMAGE AT KENYATTA NATIONAL HOSPITAL INTENSIVE CARE UNIT" (P32/4/2001)

This is to inform you that the Kenyatta National Hospital Ethical and Research Committee has reviewed and **approved** your above cited research proposal.

On behalf of the Committee I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Thank you.

Yours faithfully,

PROF. A.N. GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M. Bhatt,
Chairman, KNH-ERC,
Dept. of Medicine, UON.

Deputy Director (CS),
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The Chairman, Dept. of Surgery, UON

The Dean, Faculty of Medicine, UON