Brain death in children managed at a tertiary centre in Nigeria: a five-year review

AE Akindolire[1], AO Oyinlade[1], A Sanusi[2] and IA Lagunju[1]
Departments of Paediatrics[1] and Anaesthesia[2], College of Medicine, University of Ibadan, Ibadan, Nigeria

Abstract

Introduction: The recent advent of organ transplantation in Nigeria has emphasized the need for protocols in the diagnosis and management of brain death as is obtainable in developing countries in order to prevent waste of scarce resources and loss of potentially viable organ donors.

Aim: To determine the aetiology and outcomes of children with brain death at the University College Hospital, Ibadan.

Methods: All non-surgical paediatric patients admitted to the intensive care unit (ICU) over a five-year period were evaluated. Those with features of brain death had details of their history and physical examination findings throughout admission recorded in a proforma. The parents were counselled if the features remained consistent 24 hours after the initial assessment. Their decisions and the outcomes of the patients were documented.

Results: Thirteen patients (12.1%) out of the 108 non-surgical paediatric patients had brain death, 6(46.2%) males and 7 (61.5%) females. The major risk factor for brain death was intracranial infections, seen in 11 (84.6%). Others were bihemispheric cerebrovascular accident (7.7%) and tetralogy of Fallot (7.7%). All the parents were counselled and offered the option of withdrawal of care but none gave consent for withdrawal of care. All patients had a terminal cardiopulmonary arrest within 5 days of the first diagnosis of brain death.

Conclusion

Brain death occurred in 12.1% of non-surgical paediatric ICU admissions in our centre with intracranial infections as the leading risk factor. Our findings emphasize the need to intensify efforts and resources in the prevention of these diseases. There is also a need for development of protocols to guide the management of brain death.

Keywords: *Brain death children; organ donation; Nigeria; low resource countries*

Résumé

Contexte: L'avènement récent de la transplantation d'organes au Nigéria a souligné la nécessité de protocoles de diagnostic et de gestion de la mort cérébrale dans les pays en voie de développement afin d'éviter le gaspillage de ressources rares et la perte de donneurs d'organes potentiellement viables.

But: Pour déterminer l'étiologie et les résultats des enfants atteints de mort cérébrale au Collège Hospitalier Universitaire, Ibadan.

Méthodes: Tous les patients pédiatriques non chirurgicaux admis à l'unité de soins intensifs (USI) sur une période de cinq ans ont été évalués. Ceux avec des caractéristiques de la mort cérébrale avaient des détails de leurs antécédents et des résultats d'examen physique tout au long de l'admission enregistrés dans un formulaire. Les parents ont été conseillés si les caractéristiques restaient constantes 24 heures après l'évaluation initiale. Leurs décisions et les résultats des patients ont été documentés.

Résultats: Treize patients (12,1%) sur 108 patients pédiatriques non chirurgicaux ont eu une mort cérébrale, 6 (46,2%) garçons et 8 (61,5%) des filles. Le principal facteur de risque de mort cérébrale était les infections intracrâniennes, observées chez 11 (84,6%). D'autres étaient un accident vasculaire cérébral bi-hémisphérique (7,7%) et une tétralogie de Fallot (7,7%). Tous les parents ont été conseillés et ont offert l'option du retrait des soins, mais aucun n'a donné son consentement au retrait des soins. Tous les patients ont eu un arrêt terminal cardio-pulmonaire dans les 5 jours suivant le premier diagnostic de mort cérébrale.

Conclusion : La mort cérébrale est survenue dans 12,1% des admissions à l'USI pédiatriques non chirurgicales dans notre centre, les infections intracrâniennes étant le principal facteur de risque. Nos résultats soulignent la nécessité d'intensifier les efforts et les ressources dans la prévention de ces maladies. Il est également nécessaire de développer des protocoles pour guider la gestion de la mort cérébrale.

Correspondence: Dr. Abimbola Akindolire, Department of Paediatrics, College of Medicine, University of Ibadan, Nigeria. E-mail: abimbola_12@yahoo.com.

Mots-clés: *Enfants avec cerveau mort; don d'organe; Nigeria; pays à faibles ressources*

Introduction

Brain death is generally defined as the irreversible loss of brain function [1, 2]. The diagnosis of brain death is usually made when a patient with a known irreversible massive brain lesion is comatose, unresponsive, apnoeic, with absent brainstem reflexes all in the absence of known central nervous system depressants like hypothermia, sedatives and metabolic derangements [1].

The concept of brain death was first described in the latter half of the 20th century when cardiopulmonary resuscitation and technological advances made it possible to sustain vital body functions in the presence of irreversible brain injury. In 1967, the report from a retrospective review of 1665 patients in the United States (US) who were diagnosed brain dead concluded that electro cerebral silence in a patient who is unresponsive, apnoeic, has no brainstem reflexes and is unable to maintain circulation could diagnose brain death. [3] It was however a year later that this state was equated to death legally in the US by the Ad Hoc Committee of the Harvard Medical School. The committee defined brain death as unresponsiveness, absence of movements or breathing, absent reflexes, and a flat electroencephalogram (EEG) [3].

Many other states in the US and other developed countries subsequently developed their own definition based on these recommendations. However many countries in Africa especially sub-Saharan Africa are yet to have a legal statement on the diagnosis and declaration of brain death often leaving the physician at a loss as to what to do when faced with a patient who is brain dead [2].

This has grave implications, especially in low and middle income countries, where continuing expensive medical care in patients who cannot possibly recover, in the setting of limited resources, at the expense of those with better prognosis may not be justifiable. Furthermore a clinical diagnosis of brain death allows organ donation. The need for organ transplantation in children is increasing worldwide but there are few viable donors suitable for organ transplantation in children, therefore identifying brain death early in children could mean identifying donors suitable for children. It is especially important to have more donors suitable for children because organ transplantation procedures are now being done in the country [4, 5].

We set out to review the profile of brain death in the paediatric age group at the University College Hospital, Ibadan in order to provide some basic information on the risk factors and outcomes of brain death in affected children. The aim of the study was therefore to determine the aetiology and outcomes of children with brain death at the University College Hospital, Ibadan.

Methods

This was a prospective, longitudinal study of all paediatric patients admitted to the intensive care unit (ICU) of the University College Hospital (UCH), Ibadan, over a five-year period from June 2011- June 2016. UCH is an 850 bedded tertiary health facility located in Ibadan, the largest city in the South Western part of Nigeria with a population of 2,550,593.[6] It serves as a referral centre to all health care facilities in the city and other neighbouring towns and states and it also accepts self referrals. University College Hospital has a twelve-bedded general ICU where all critically ill patients are managed. The ICU care is from out of pocket payments by caregivers.

All non surgical patients were carefully evaluated at admission and daily during the period of admission in ICU for features of brain death. Diagnostic criteria for brain death were based on the recommendations of the American Academy of Neurology.[7] A diagnosis of brain death was made in the presence of deep unresponsive coma, apnoea and absent brainstem reflexes in a patient with a known irreversible brain lesion.[7] The children were considered eligible for recruitment if they had all the features stated above; in the absence of known central nervous system depressants like hypothermia, sedatives and metabolic derangements [7]

At first diagnosis of brain death, details of clinical history and full physical examination findings, including the state of responsiveness determined by the Glasgow coma score, brainstem reflexes, temperature and blood pressure were recorded. The medical discipline of the first physician to make the diagnosis was noted, i.e. anaesthetist, intensivist or paediatric neurologist. All cases were on mechanical ventilation and had continuous monitoring of all vital signs. During the observation period, care was taken to ensure that the patient had normal temperature and electrolytes, and their circulation optimized. A repeat assessment was carried out 24 hours after the initial assessment and the diagnosis of brain death was confirmed when the features remained consistent. Personnel responsible for the second assessment were also documented.

In line with the hospital protocol, the parents/ caregivers were counselled by a team comprising of the intensive care unit nurse, the anaesthetist/ intensivist, the paediatric neurologist and the medical

social workers. Decisions of the caregivers with respect to continuing ventilator support was documented. Outcomes following diagnosis of brain death were recorded.

Results

General characteristics

A total number of 2,240 patients were admitted into the ICU during the study period. There were 225 children, 108 of whom were non surgical cases. The most common reasons for ICU admission among the non surgical paediatric patients were tetanus (21.3%), congenital heart disease (20.3%) and meningitis (15.6%) as shown in Table 1.

Table 1: Diagnoses of non-surgical paediatric patients admitted into the intensive care unit

Cases	Number of patients (%)
Tetanus	23(21.3)
Congenital heart disease	22(20.3)
Meningitis	17(15.6)
Pneumonia	8(7.4)
Septicaemia	6(5.6)
Severe malaria	6(5.6)
Complications of sickle cell disease	6(5.6)
Infectious pericarditis	4(3.7)
Corrosive poisoning	3(2.8)
Upper respiratory tract obstruction	3(2.8)
Acute flaccid paralysis	2(1.9)
Others	8(7.4)
Total	108(100.0)

Table 2: Age and gender distribution of children with brain death seen in the intensive care unit

Age in months	Sex	
	Male n (%)	Female n (%)
<1 year	0	1(7.7)
1 – 5 years	2(15.4)	4(30.8)
>5 years	4(30.8)	2(15.4)
Total	6(46.2)	7(53.8)

Risk factors for brain death

Thirteen non-surgical paediatric patients were diagnosed with brain death over the study period; 6 (46.2%) males and 7 (53.8%) females. Their ages ranged from 11 months to 11 years. Table 2 shows the age and gender distribution of the cases. Ten (76.9%) of them were comatose on admission while the remaining 3 (23.1%) were conscious on admission. All the patients were transferred to the ICU following deterioration in their clinical status.

Diagnosis

The underlying clinical condition that resulted in brain death was identified in all cases. Intracranial infections, seen in 11 (84.6%) of the cases represented the leading risk factor for brain death in the cohort; these consisted of 7 cases of bacterial meningitis, 2 cases of viral encephalitis and 2 case of cerebral malaria. All had features of raised intracranial pressure. There was one case each of bihemispheric cerebrovascular accident in a 10 year old with sickle cell anaemia and a 17 month old with tetralogy of Fallot with severe hypoxia from tet spells. Table 3 shows the clinical profile and risk factors for brain death in the cohort.

Table 3: Primary diagnoses in the 13 patients with brain death admitted into the intensive care unit

Cases	Number of patients (%)
Pyogenic Meningitis	7(53.8)
Cerebral Malaria	2(15.4)
Varicella Encephalitis	1(7.7)
Viral Encephalitis	1(7.7)
Cerebrovascular accident	1(7.7)
Tet Spells	1(7.7)
Total	13(100.0%)

Caregivers' perception on brain death

All the caregivers were counselled on the clinical state, course and prognosis of brain death. All were given the opportunity to decide on the withdrawal of ventilator and support. None of the caregivers opted for withdrawal of care. They all decided for continued ventilatory support till a definite outcome was determined, all citing religious belief in the miraculous as their reasons.

Outcomes

All patients had a terminal cardiopulmonary arrest within 5 days of the first diagnosis of brain death. Interval between first assessment and death ranged from 10 hours to 5 days, with a median duration of 51 hours.

Discussion

The implications of declaring a patient brain dead have far reaching consequences for the family and the physician. Most countries in Europe, Asia and South America therefore have well defined criteria for the diagnosis of brain death as well as laws to

govern both the diagnosis and what happens after the diagnosis is made [2, 8]. In Africa however, especially in sub-Saharan Africa most countries do not have protocols or guidelines to follow in the diagnosis and management of brain death. In Nigeria, there is no consensus yet to guide the diagnosis of brain death. Our protocol in our centre is guided by the American Academy of Neurology (AAN) protocol for diagnosis of brain death [7].

It has become important to have guidelines on the diagnosis of brain death since many hospitals now have staff who are trained in cardiopulmonary resuscitation [9]. In addition, tertiary centres now have ventilators and are therefore able to maintain respiration and keep the heart beating in the absence of brain function [10]. Having clear guidelines will help the physician to identify when a patient on mechanical support suffers brain death and to follow the appropriate steps. This has major implications for the optimal allocation and deployment of the scarce resources as is seen in many resource-poor countries of the world. In this review unresponsiveness, apnoea, absent brainstem reflexes in the absence of confounders such as hypothermia and sedatives and in a patient with a known cause of brain injury was diagnosed as brain dead. These criteria are based on parameters developed by the Harvard committee which most states in the US have based their guidelines on except for the fact that no EEG was done in this study because the consensus in most countries now is that brain death is a clinical diagnosis and does not require any investigations except in neonates [11].

There is a paucity of data from developing countries on the risk factors for brain death. In this review, majority (78.6%) of the cases were due to intracranial infections, there was however one subject who had congenital heart disease, one with tracheoesophageal fistula and another with cerebrovascular accident. This high percentage of patients with intracranial infections is consistent with findings from developed world where the most common medical cause for brain death was intracranial infections [12]. This therefore brings to the fore the need to increase efforts and resources directed at the prevention of these infections.

The diagnosis of brain death is usually followed by a series of serious decision making. It is usually very emotional for the parents and family and often these emotions have to herald not just the decision to withdraw support but also the decision to donate or not to donate organs. In a setting where there are no definite laws and the sympathy usually lies with the family of the patient, these decisions are left solely in the hands of the family rather than having protocols which the physicians can follow. As seen in this review however, despite the fact that these patients were all brain dead, which should be synonymous with death legally, because there are no laws in place to guide and guard the physicians, withdrawal of care was impossible leading to an enormous waste of resources which could have been put to better use. Some countries in sub Saharan Africa have recognised the need for protocols and policy regarding brain death in order to prevent waste of resources and prolonged suffering of patient's relatives [13]. It is no surprise however that these parents refused to give consent for withdrawal of care as most people in Nigeria have strong religious beliefs that either prohibits from any interference in the process of death or gives hope in miraculous recovery. The impact of religious beliefs and ethnic differences in these processes have been well documented [5].

Another major reason why making the diagnosis of brain death early is important is to allow for prompt identification of suitable organ donors and those vital organs could be ethically obtained for transplantation. This has become quite important because the country now has a number of centres where kidney transplantations take place [4]. Identifying these viable donors early will likely reduce the mortality from end stage renal failure and improve the outcomes for end stage renal disease which currently has grave prognosis in Nigeria.

All the patients proceeded to cardiac arrest within a few days despite efforts to optimize circulation. This is similar to the previously reported 48 to 72 hours in adults and up to 10 days in children.

Conclusion

Intracranial infections were the most common aetiology of brain death and all patients had a cardiac arrest within five days of diagnosis. All caregivers refused to give consent for withdrawal of care, this implies that the concept of brain death may not be well accepted in this environment although there is a need for further studies evaluating the effect of socio cultural and religious beliefs in the acceptance of brain death. The focus of such studies should also include generating data that can be used in policy making and protocol development in brain death in children in this environment.

References

1. Lorry R. F and Mathers LH. Withdrawal or Withholding of Life Support, Brain Death, and Organ Procurement 2011. In: Nelson Textbook

of Pediatrics [Internet]. Philadelphia: Saunders. 19th. [340-342].
2. Wijdicks EF. Brain death worldwide Accepted fact but no global consensus in diagnostic criteria. Neurology. 2002;58(1):20-25.
3. Beecher H. Report of the ad hoc committee of the Harvard Medical School to examine the definition of brain death: The definition of irreversible coma. Transplantation. 1969;7(3):204.
4. Arogundade F.A. Kidney transplantation in a low-resource setting: Nigeria experience. International Society of Nephrology, 2013.
5. Tsai E, Shemie SD, Cox PN, *et al.* Organ donation in children: Role of the pediatric intensive care unit. Pediatric Critical Care Medicine. 2000;1(2):156-160.
6. National Population Comission. National Census In: National Population Commission, editor. Ibadan2006.
7. Nakagawa TA, Ashwal S, Mathur M and Mysore M. Guidelines for the determination of brain death in infants and children: An Update of the 1987 Task Force Recommendations—Executive Summary. Annals of Neurology. 2012;71(4):573-585.
8. Van Norman GA. A Matter of Life and Death What Every Anesthesiologist Should Know about the Medical, Legal, and Ethical Aspects of Declaring Brain Death. Anesthesiology: The Journal of the American Society of Anesthesiologists. 1999;91(1):275-287.
9. Desalu I, Kushimo O and Akinlaja O. Adherence to CPR guidelines during perioperative cardiac arrest in a developing country. Resuscitation year 69 (3):517-20.
10. Okafor U. Challenges in critical care services in Sub-Saharan Africa: Perspectives from Nigeria. Indian Journal of Critical Care Medicine. 2009;13(1):25-27.
11. Mohandas A and Chou SN. Brain death: a clinical and pathological study. Journal of neurosurgery. 1971;35(2):211-218.
12. Ashwal S and Serna-Fonseca T. Brain death in infants and children. Critical care nurse. 2006;26(2):117-128.
13. Waweru-Siika W, Clement ME, Lukoko L, *et al.* Brain death determination: the imperative for policy and legal initiatives in Sub-Saharan Africa. Global public health. 2017;12(5):589-600.