Pediatric Experience With Brain Death Determination

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A retrospective study of the experience at the University Pediatric Hospital during a six-year period when 2529 patients were admitted to the Pediatric Intensive Care Unit (PICU) and 80 were diagnosed with brain death. Etiologic causes, age and sex distribution and use of confirmatory studies were evaluated. The specific criterias for brain death determination in children are discussed and it was found that 3.1% of all the admissions to PICU were diagnosed with brain death. This diagnosis was most common in the 6 to 12 year old children (35%) and in infants younger than 2 years of age (30%). Trauma accounted for 41.0% of the cases. In babies less than 6 months of age, 71.4% were battered. Only 11% accepted organ donation.

Key word: Brain death, Diagnosis, Pediatric etiology, Apnea test, Electroencephalogram, Brain death criteria, Pediatric intensive care, Organ donation, Brain radio nuclide scintigraphy.

Brain death is defined as the irreversible loss of both cortical and brainstem activity. It is clinically determined based on established criteria and is not dependent on the cause of brain injury (1,2,3). The first definition of brain death was elaborated in 1968 by the Report of the *Ad Hoc* Committee of Harvard Medical School (4). Shortly after, in a collaborative study the National Institutes of Neurologic Diseases and Stroke established brain death criteria. These were widely adopted and more recently, the American Academy of Neurology published standards for the diagnosis of brain death (2,3).

To diagnose brain death the clinician must prove the absence of cortical function in the presence of deep coma, with no response to noxious or other stimuli. Absent brainstem functions, including testing for pupillary, light, corneal, oculocephalic, oculovestibular, oropharyngeal, and respiratory reflexes, must be determined. Drug intoxication, metabolic derangements, profound hypothermia (less than 33°C), and shock, which may cause reversible loss of specific brainstem reflexes, have to be excluded. Pupils of brain dead patients may be mid-sized and fixed and not necessarily fixed and dilated as previously thought. It is also mandatory to perform the apnea test (that includes at least a 10-minute pre-oxygenation with 100% oxygen allowing the $PaCO_2$ to increase to more than 60 and/or 20 mmHg above baseline), demonstrating no spontaneous respiratory movements (2).

Corroborative studies for brain death determination may include isoelectric EEG and absent cerebral blood flow on angiography or nuclear studies. These ancillary tests are confirmatory but are not essential for the diagnosis of brain death in patients older than one year. Nevertheless, they are objective measures that help parents understand the diagnosis of brain death in children. Brain death certification requires two physicians, one should be the treating physician, and the other, ideally, a neuroscience specialist (neurologist or neurosurgeon), but in the absence of such, another physician, internist, pediatrician, surgeon or anesthesiologist may suffice.

The University Pediatric Hospital is the only supratertiary referral center for pediatric trauma in Puerto Rico and the Caribbean. Since 1976, at the Pediatric Intensive Care Unit (PICU), the term brain death has been employed in death certificates and mortality reports. Twelve years ago the Institutional Ethics Committee reviewed and adopted the National guidelines for the determination of brain death in children (5,6). In this article we review our experience with brain death determination, its incidence and etiology in the Puerto Rican pediatric population.

Methodology

We retrospectively reviewed the records of all patients admitted to PICU from October 1, 1995 to September 30, 2001 who were diagnosed with brain death. During this period a total of 2529 patients were admitted to the unit,

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and eighty patients were diagnosed as Brain Dead (3.1% incidence).

The records of all 80 patients with the diagnosis of brain death were reviewed. Management was given according to the current established protocol in the unit for brain protection. All patients were mechanically ventilated. Continuous neurological evaluation was performed and charted every two hours. Sixty-seven patients (83.6%) required inotropic support and in eleven (16%) barbiturates had been used to induce barbiturate coma. Supportive treatment had continued until brain death certification was documented on the medical record. The diagnosis of brain death was done following the institutional guidelines.

When clinical signs of brain death were identified, all sedatives, analgesics, neuromuscular blocking agents, barbiturates, and anticonvulsants were discontinued. Anticonvulsant and narcotic drug levels were measured to rule out intoxication. Two complete neurological examinations were performed, one by the primary pediatrician (the pediatric intensivist) and another by a neurosurgeon or neurologist to determine brain death. Electro encephalography and brain flow studies, although not mandatory, were ordered on many occasions to confirm the clinical examination. Brain death diagnosis was explained to parents and the possibility of organ donation was discussed with them. The primary physician discontinued respiratory and hemodynamic support.

Results

During the six years study period, 3.1% of the admissions (80 patients) met the criteria for brain death. These cases represent 27.6 % of the total mortality for the same period. Clinical signs of brain death were present at the time of admission in 34.7% of the patients. Fifty-four were males and twenty-six were females, 2.1:1 ratio. The age ranged from 1 day to 16 years old, mean age was 84.8 months, ± 61.9 months (SD). Brain death was most frequently diagnosed in the 6 to 12 years old group (35%), followed by infants less than 24 months of age (30%). See Table 1.

Table 1. Age and Sex Distribution

Age	No	%	Males	Females
< 1 m/o	1		1	
1-6 m/o	6	7.5	4	2
7-24 m/o	17	21.2	12	5
2-5 y/o	11	13.6	7	4
6-12 y/o	28	35	17	11
>12 y/o	17	21.2	13	4
	80		**54(67.5%)**	**26(32.5%)**

Eight cases had primary cerebral pathology, six with space occupying lesions and 2 with a malfunctioning ventriculoperitoneal shunt. The remaining 72 cases were healthy children prior to the event that lead to brain death.

Trauma was the most frequent etiologic diagnosis (41.0%), non-intentional head trauma in 27 cases and intentional trauma in six children (age's 1 day to 24 months). See Table 2.

Table 2. Brain Death Etiology

Etiology of coma	No	Percent (%)
Trauma non-intentional	27	33
Intentional trauma	6	8
Anoxic-ischemic	18	22
Intracerebral hemorrhage	10	12
Space occupying lesion	6	8
Encephalopathy	3	4
Status epilepticus	4	5
Others	6	8

In 18 patients the neurological deterioration that led to brain death was secondary to an ischemic-hypoxic event. Ten of them had experienced a cardio-respiratory arrest (CRA) prior to admission. Three patients with history of bronchial asthma developed CRA at home, three occurred in battered children and in three other patients, at the time of a drowning event. Five cases had exhibited several forms of respiratory pathology, including one with upper airway obstruction, due to a foreign body aspiration, that developed CRA at home. Corroborative studies for brain death certification (EEG and brain flow studies) were done in 58 patients (72.5 %). In 9 of 11 patients treated with barbiturates to control increased Intracranial pressure, the cerebral blood flow study confirmed absent cerebral perfusion, the other two died before the study could be performed. In six patients who were too unstable for transport to the brain scan, repeated EEGs, 24 hours apart, were obtained to confirm the clinical diagnosis. No corroborative studies were done in 16 cases, due to patient demise.

Brain death was diagnosed in 7 patients younger than 6 months of age. Five of these babies (71.4%) were battered children (Table3). The EEG was isoelectric in all patients and the cerebral blood flow (CBF) study was consistent with brain death in 4.

Discontinuation of the respiratory support was done after one or two family meetings. The significance of brain death and the confirmatory studies were presented sequentially to the family. This process varied from several hours to 2 days, depending on the parent's acceptance of

the condition. Mean PICU stay was 4.4 days, with a range of 1 to 17 days. This period represents the total hospitalization length, not the time after the patient was declared brain dead. In 9 patients the family agreed to organ donation (11.3%). Physiologic support was continued according to the protocol of the Organ Donation Program.

Table 3. Etiology and corroborative studies in children less than 6 months old

Age	Etiology	CBF	EEG
1 day	Head trauma, battered	X	X
4 mo.	Intracranial hemorrhage	-	X
3 mo.	Head trauma, subdural, battered	-	X
2 ½ mo.	Bronchiolitis, S/P CRA	X	X
2 mo.	Shaken baby syndrome, S/P CRA	X	X
3 mo.	Battered child, S/P CRA	X	X
5 mo.	Head trauma, battered child	-	X

Discussion

Children admitted to the intensive care unit with neurological dysfunction are followed hourly with the Glasgow Coma Scale (GCS), or the modified version for infants. The GCS provides the required objective neurological assessment to monitor and manage acute neurological changes. It also helps to define the moment when the patient shows clinical evidence of absent cortical and brain stem functions. When such condition happens, barbiturates, sedatives, anticonvulsants, analgesics and paralyzing agents are discontinued, and their levels measured. EEG and neurological evaluation, including the apnea test, are requested. Brain radio nuclide scintigraphy is also ordered. The 4-vessels contrast angiography used to be the gold standard, but we currently employ the brain scan because it is less invasive and cumbersome (7). Although corroborative studies are not longer required for brain death determination, we used them in two thirds of our cases. This same pattern is published in similar studies.

We report an overall incidence of brain death of 3.1% of all admissions to PICU during the six- year study period, representing 27.6% mortality. Staworn et at. reported a 0.9% incidence, accounting for 11% of their mortality (8). In 1988, in a prior unpublished study at our Unit, we evaluated 115 patients with brain death out of 2711 admissions during a 5.5-year period. A 4.2% incidence was then found. The higher incidence of brain death in our admissions may reflect several realities of our unit: it is the only supraterciary referral center for pediatric trauma and burns in our island and in the Caribbean. Since it has the needed resources for brain death determination some patients are transported to our unit for the sole purpose of brain death confirmation.

Ruiz-López, et al described a series of 51 cases of brain death, 55.2% males and 49.8% females with a similar age distribution as our study (9). Interestingly, their patients were younger than ours, 29.4% of their cases were less than 1-year-old, yet there were only 5 cases older than 14 years old. In another study of 125 cases the age distribution was between 18 days to 17 years old, and patients younger than 2 years predominated (10). It is a well- recognized trend that as children grow, males are more prone to accidental injuries and death. Our population showed a male preponderance compatible with the higher age group of our patients.

As has been described by others, head trauma was the most frequent etiology leading to brain death in our patients. In Ruiz-López et al series it accounted for 31.3 % of the cases. Drowning/near drowning was the second cause of death in Staworn's and infection in 34% of Ruiz-García et al, series. In our series back in 1988 there were 7 cases of *Haemophilus influenzae* meningitis causing brain death. With the subsequent introduction of vaccination against *H. influenzae*, in our present series, there are only two cases due to meningitis, but now due to Streptococcus pneumonia.

In 1983, for the first time, the Report by the President's Commission for the study of Ethical Problems in Medicine included children over 5 years old in brain death determination, (11). Although criteria for determining brain death have been gradually refined over the years, several findings have always been found indispensable: absent response to any stimuli, no spontaneous breathing or other brain stem reflexes, and most important, evidence that the loss of these functions is irreversible. It is also essential to determine the cause of the neurological dysfunction. This can be corroborated through clinical findings and neuroimaging studies with sufficient evidence to explain the neurological status. A period of observation sufficient to confirm the irreversibility of functional loss and the exclusion of medical conditions like " lock in" syndrome in pontine infarction, brain stem encephalitis, drug intoxication, and body temperature of less than 90^{0}F (32.2^{0}C) should be offered (12,13).

The value of the EEG in the determination of brain death has been questioned extensively, claiming that it lacks sensitivity and specificity (9). Grigg et al, published a series of 56 clinically brain death patients, between the ages of 16 months to 82 years, 19.6% had some significant electrical activity in their EEG while half of them had a brain scintigraphy showing no perfusion (14). Neonates may exhibit electro cerebral silence, for a prolonged period

of time, after suffering an ischemic insult. A study of 20 neonates with severe encephalopathy, 75% showed Electro cerebral silence after which 25% recovered some type of function, but only 10% exhibited clinically significant improvement(15). Pampiglione et al evaluated 2180 EEG in 363 resuscitated children and concluded that there was "little difficulty in predicting irreversible loss of cerebral function if the electro-cerebral silence persisted for 6-12 hours". We continue to recommend EEG evaluation in all patients with clinical brain death. In our experience, patients who were clinically brain dead, and whose EEG showed some activity, when repeated, within 24 hours, became isoelectric.

The American Academy of Pediatrics in 1987 introduced several modifications in brain death determination in children and established the observation period required according to their age:

1) The patient must be older than 7 days and not premature.
2) The observation period and confirmatory tests to be ordered will vary according to patient's age:

    a. Babies 7 days to 2 months old require two neurological evaluations 48 hours apart and one confirmatory test (EEG, brain flow, PET scan or angiography).
    b. Infants 2 months old to 1 year of age require two examinations 24 hours apart and one confirmatory test.
    c. Children older than 1 year old will only need two neurological examination 12 to 24 hours apart and no confirmatory study will be required if the cause of death is known.

In our experience most patients are certified as brain dead in 48 hours. The duration of observation has been a matter of controversy due to the apparently inappropriate use of resources. As stated by Postner and Plum, brain death patients will invariably die, no matter what methods of cardio-respiratory support are given. Yet, this period is crucial for the parents of a brain dead child, who suddenly must face the reality of the unexpected death of their previously healthy child. Each family is unique in their needs and the intensive care staff has to be sensitive and provide the individual support they require.

There has been a debate on how to deliver the information of the death of a patient based on neurological criteria. Most authors agree that even physicians have problems understanding the concept of brain death. Much education is needed in our community, with strong religious and cultural believes, to accept brain death as an irreversible process. Also, the need for organ donation should be aggressively addressed. In the population studied only 11% of our cases accepted organ donation, a trend that has remained the same through the years.

Resumen

Un estudio retrospectivo de 80 pacientes con diagnóstico de muerte cerebral, admitidos a la unidad de cuidado intensivo del Hospital Pediátrico Universitario, de un total de 2529 admisiones durante un período de seis años consecutivos. Se evaluó la etiología, distribución por edad y sexo y estudios confirmatorios empleados. Se discuten los criterios específicos pediátricos para determinar muerte cerebral y se concluyó que 3.1% del total de admisiones fueron diagnosticadas con muerte cerebral. La muerte cerebral fue más frecuentemente diagnosticada entre las edades de 6 a 12 años (35%), seguido por los menores de 2 años (30%). El trauma fue la causa más común de muerte cerebral (41.0%). El síndrome de niño maltratado fue identificado en 71.4% de los casos menores de 6 meses de edad. La donación de órganos se logró en 11% de los casos de muerte cerebral.

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