Brain death and organ donation of children

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We aimed to define the demographic characteristics, clinical features and outcome of patients with brain death, and to emphasize the importance of organ donation from children. Data for the period from September 2009 to October 2012 were collected retrospectively. Twenty children who were diagnosed as brain death were included. Data including demographics, major cause leading to brain death, duration of brain death evaluation, ancillary tests used to confirm brain death, complications and outcome, duration of hospitalization and organ donation were collected for statistical evaluation. The mean age was 6.2 years, and the male/female ratio 1.85. The major cause leading to brain death was most often traumatic brain injury, seen in 11 patients (55%). The mean duration of brain death evaluation was 6.7 and 1.7 days in Centers I and II respectively. The mean duration of hospitalization was 12.5 days. Electroencephalography (EEG) was used in 18 patients (90%). Complications included hyperglycemia in 13 cases and diabetes incipitus in 7 cases (65% and 35%, respectively). Mean duration of survival was 9.8 days. In Center I, one of the patients' parents gave consent to organ donation, while four parents in Center II agreed to organ donation. The study demonstrated that the duration of brain death evaluation was longer in Center I than in Center II ($p<0.05$). When both centers were compared, there was no significant difference in regard to obtaining consent for organ donation, survival after diagnosis of brain death and length of stay in the PICU ($p>0.05$). Early diagnosis of brain death and prompt evaluation of patients by ICU physicians once the diagnosis is taken into consideration will probably yield better organs and reduce costs. Training PICU physicians, nurses and organ donation coordinators, and increasing children's awareness of the need for organ donation via means of public communication may increase families' rate of agreement to organ donation in the future.

Key words: ***brain death, children, organ donation, pediatric intensive care unit.***

Brain death is defined as the cessation of cerebral and brainstem functions. It is a clinical diagnosis made by a series of brainstem reflex tests in the absence of factors such as endogenous or exogenous poisons, toxins or hypothermia that might confound the clinical picture[1-4]. The etiology of brain death in children is mainly due to traumatic brain injury[5-7]. The diagnosis has three important components: demonstration of irreversible coma/unresponsiveness; absence of brainstem reflexes; and apnea. These three components should be reconfirmed after an observation period. The duration of the observation period is longer in children, which is one of the main differences in establishing the diagnosis in children as compared to adults[2,4-5,8].

In our country, the law allowing transplantation using organs from donors diagnosed with brain death was approved in 1979[9]. Although Turkey was one of the first countries to establish a legal framework for organ transplantation, and also had facilities capable of performing the procedure, the number of brain death declarations has been relatively low compared with the rest of the world.

Studies of organ donation in children are rare. As a consequence of the shortage of organs available to meet the demand for transplantation, children are dying while waiting for transplants; it has been found that 30-50% of children under 2 years of age die during the waiting period for organ transplantation. Therefore, the diagnosis of brain death and the care of the donor organs are extremely important in the case of children[6,10-13]. The current practice in the developing world for determining brain death in the pediatric population is not well characterized. The aim of this study was to define the demographic characteristics, clinical features and outcomes of patients with brain death and to emphasize the importance of organ donation in children.

Material and Methods

After approval from the institutional ethics committee, the study was performed in two major multidiciplinary tertiary care hospitals in the capital city of the country. Center I has 14 pediatric intensive care beds. Its pediatric intensive care unit is one of the largest tertiary referral centers in the nation; it receives referrals from throughout the country and admits nearly 450 patients per year from all specialties except for trauma patients. Center II is one of the few trauma centers designated by the Ministry of Health and accepts patients from all age groups, including adults. It has eight intensive care units for the following areas/specialties: intensive care, anesthesiology and reanimation (12 beds), internal medicine (10 beds), coronary care (12 beds), neurology (6 beds), emergency care (10 beds), cardiovascular surgery (6 beds), general surgery (5 beds) and neurosurgery (6 beds). Both hospitals have accredited residency programs. The hospital information database systems were used to collect data on all patients with a diagnosis of brain death during the period from September 2009 to October 2012. A total of 20 brain death patients were identified for the purposes of the study. The medical records of patients who were diagnosed with brain death were evaluated and retrospective chart reviews were performed. Brain death patients were identified using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) principal diagnosis codes[14]. Patients between 1 month and 18 years of age were included in the study. Data comprising demographics, major cause leading to brain death, duration of brain death evaluation and hospitalization, ancillary tests used to confirm brain death, complications and outcome of brain-dead patients, including the status of survival, and organ donation were collected and documented retrospectively for statistical evaluation. Patients younger than 1 month and older than 18 years of age were excluded from the study.

The criteria for diagnosis of brain death were defined by the guidelines[4]. The law in our country also requires the confirmation of irreversible coma, absence of brainstem reflexes and a positive apnea test in a normothermic, nondrugged patient. Laboratory tests were done in all patients to rule out metabolic causes of coma. In each hospital, the final decision regarding brain death had to be confirmed by a committee consisting of four physicians from different specialties including pediatric neurology, neurosurgery, anesthesiology and pediatric cardiology. Confirmatory ancillary tests were performed based on the committee's judgment[9,15]. Relatives of patients were informed about the declaration of brain death by an experienced ICU physician who was working in the unit. The request for organ donation was made by the organ donation coordinator at each hospital.

Statistical analysis

Descriptive statistics are summarized in the table. Using Kolmogorov-Smirnov and Shapiro-Wilk tests, none of the variables were normally distributed. Therefore the data were analyzed using nonparametric tests. The Mann-Whitney U test was used to compare continuous variables. All of the data were analyzed using SPSS for Windows version 17 (SPSS Inc, Chicago, IL). Data on Center I and Center II were compared; $p < 0.05$ was considered statistically significant.

Results

Data from a total of 20 brain death patients were used in the study. The patients were evenly distributed between the centers (10 from Center I and 10 from Center II). The male to female ratio was 1.85, with 13 male (65%) and 7 female patients (35%). The mean age of the patients was 6.2±5.3 (min: 0.8, max: 17.5, median: 3.8) years. The major cause leading to brain death was traumatic brain injury in 11 patients (55%), intracranial bleeding in 4 (20%), intracranial infection in 3 (15%), intracranial tumor in 1 (5%) and chemical exposure in 1 (5%) (Table I). The mean duration of hospitalization was 12.5±10.7 (min: 3, max: 40, median: 7.5) days. The mean duration of brain death evaluation was 6.7±6.4 (min: 1, max: 20, median: 4) days in Center I and 1.7±1 (min: 1,max: 4, median:

1) days in Center II. Electroencephalography was the most commonly utilized ancillary test, conducted in 18 patients (90%). This was followed by MR/CT angiography in 2 patients (10%), DSA in 2 (10%) and Doppler USG in 1 (5%). Complications after the declaration of brain death included diabetes incipitus in 7 cases (35%) and hyperglycemia in 13 (65%) (Table II). Mean duration of survival after the diagnosis of brain death was 9.8±9.4 days (min: 1, max: 28, median: 6). All of the families were approached for organ donation, and consent was obtained in 25% (5/20) of those who were asked. All of the patients were medically suitable, except for one who had an overwhelming infection. In Center I, the parents of one patient gave consent for organ donation, though unfortunately this was the patient who was not suitable for donation, while the parents of four patients in Center II agreed to organ donation, with transplantation subsequently carried out. The study demonstrated that the duration of brain death evaluation was longer in Center I than in Center II, and this was statistically significant, with $p=0.007$ ($p<0.05$). When the centers were compared to each other, there was no significant difference in regard to obtaining consent for organ donation, survival after the diagnosis of brain death and length of stay in the ICU ($p>0.05$).

Discussion

Although there exists plenty of literature on trends in determining brain death, there are few studies in the pediatric population, and information concerning this subject is even scarcer in the case of the developing world. Therefore, the present study was conducted to define the clinical features and outcome of pediatric patients with brain death, emphasizing the importance of organ donation in children. There were 13 male (65%) and 7 female (35%) patients. These findings were similar to the literature, where there are figures of 56% male and 44% female[6,16]. In one study, females exceeded males, at 51.3%[7].

In our results, the mean age of the patients was 6.2 years. Similar to this finding, the mean age was 5.8 years[6] and 7 and 7.8 years in some other studies[7,16]. In one study, it was as old as 13.5 years (median:16)[17], while in another study 53.8% of the patients were over 5 years old[7]. Ruiz Garcia et al.[18], on the other hand, found a predominance of children who were less than 2 years old. It is difficult to compare age distributions between studies, because the inclusion criteria are different in each one.

According to our results, the cause of brain death was traumatic brain injury in 11 (55%), intracranial bleeding in 4 (20%) and intracranial infection in 3 (15%) of the patients. In one study, acute neurosurgical lesion was present in 46% of patients, followed by hypoxic ischemic encephalopathy in 33% and infection in 12%[6]. In most studies, the most common finding in children was traumatic brain injury[5-7,16]. Complications after the declaration of brain death included diabetes incipitus in 35% of our patients, the same as in other studies[5,12]. Electroencephalography was the most commonly utilized ancillary test, employed in 18 (90%)

Table I. Demographic Characteristics of Patients.

Variables		(n=20)
Age (years), Mean±SD (median)		6.2±5.3 (3.8)
Gender, Male, n (%)		13 (65)
Female, n (%)		7 (35)
Major cause leading to brain death, n (%)		
Traumatic brain injury		11 (55)
Intracranial bleeding		4 (20)
Intracranial infection		3 (15)
Intracranial tumor		1 (5)
Chemical exposure		1 (5)
Duration of brain death evaluation (days),		
Mean±SD(median)	Center I	6.7±6.4 (4)
	Center II	1.7±1 (1)
Duration of hospitalization (days), Mean±SD (median)		12.5±10.7 (7.5)
Duration of survival after diagnosis of brain death (days), Mean±SD (median)		9.8±9.4 (6)
Organ donation, n (%)		5 (25)

Table II. Causes of Brain Death in Two Centers

CENTER I	Age (years)	Gender	Diagnosis	Ancillary tests	Duration of diagnosis of brain death (days)	Survival after the diagnosis (days)	Complications
Patient 1	1	M	Intracranial infection, Intracranial bleeding	Apnea test	4	3	Hyperglycemia, brain edema
Patient 2	0.9	M	Road accident, Traumatic brain injury	Apnea test, EEG, MR angiography	12	28	Hyperglycemia, diabetes incipitus
Patient 3	14	M	Intracranial infection	Apnea test, EEG	14	9	Hyperglycemia, diabetes incipitus
Patient 4*	11.5	F	Myelomeningocele, Hydrocephalus, Intracranial infection	Apnea test, EEG	2	1	Ø
Patient 5	2.9	F	Chemical exposure, Myocardial damage	Apnea test, EEG	5	1	Hyperglycemia, diabetes incipitus
Patient 6	5.9	M	Road accident, Traumatic brain injury	Apnea test, EEG	2	15	Hyperglycemia, diabetes incipitus
Patient 7	0.7	F	Intracranial bleeding, Carditis of acute rheumatic fever	Apnea test	4	1	Ø
Patient 8	7	M	Intracranial tumor, Medulloblastoma	Apnea test, EEG	3	1	Ø
Patient 9	2.5	F	Intracranial bleeding, Arteriovenous malformation	Apnea test	1	2	Ø
Patient 10	1.1	M	Intracranial bleeding, Subdural hematoma	Apnea test, EEG, Contrast cranial tomography	20	1	Diabetes incipitus, brain edema
CENTER II Patient 11*	16.5	M	Traumatic brain injury, Suicide, Fall from height	Apnea test, EEG	1	2	Ø
Patient 12	17.5	M	Road accident, Traumatic brain injury, Subdural hematoma	Apnea test, EEG	2	4	Ø

Patient 13*	3.5	F	Road accident, Traumatic brain injury, Subdural hematoma	Apnea test, EEG, MR angiography, Selective cerebral angiography	1	23	Hyperglycemia, diabetes incipitus
Patient 14*	7	M	Road accident,Traumatic brain injury	Apnea test, EEG, Selective cerebral angiography	1	1	Hyperglycemia
Patient 15	3.2	M	Road accident, Traumatic brain injury	Apnea test, EEG	1	3	Hyperglycemia
Patient 16	9.3	F	Road accident, Traumatic brain injury	Apnea test	1	8	Hyperglycemia
Patient 17	4	F	Traumatic brain injury, Accidental fall from height	Apnea test, EEG	1	1	Hyperglycemia
Patient 18*	11	M	Road accident, Traumatic brain injury, Subarachnoidal hemorrhage	Apnea test	2	7	Hyperglycemia
Patient 19	2.8	M	Road accident, Traumatic brain injury, Subarachnoidal hemorrhage	Apnea test, EEG	3	4	Hyperglycemia, diabetes incipitus
Patient 20	2.5	M	Intracranial Infection/Postoperative Abcess	Apnea test, EEG	4	1	Hyperglycemia

*Patients for whom organ donation was accepted of patients, the same as in the literature[5,18]. It was followed by MR/CT angiography, DSA and Doppler USG. EEG, cerebral angiography, radionuclide angiography and transcranial doppler sonography are neuroimaging techniques used to document abscence of cerebral blood flow[5]. Transcranial Doppler monitoring of pediatric patients is of value in identifying patients who have severe cerebral compromise progressing to brain death[5,19]. We believe that neurologic examination is the gold standard, and that an apnea test is sufficient for diagnosis of brain death; in our experience, performing EEG entails technical difficulties given that patients are mechanically ventilated. However, the Ministry of Health requires an ancillary test, either MR/CT angiography or cranial Doppler USG, along with an apnea test for diagnosis of brain death.

In most children, brain death is declared and confirmed within the first 2 days of hospitalization, as was the case in our findings[5]. In our study, the mean duration of brain death evaluation was 4.2 days, with a median of 2 days. In another study this was 6 days, with a median of 3 days[17].

Our study has yielded some key findings, the first being that the number of brain death patients was few in both centers. The current Ministry of Health standards in our country require the declaration of one brain death patient per bed per year for intensive care units to be designated as such. In addition, according to the most recent regulation, one pediatric intensivist/anesthetist and one pediatric neurology specialist/neurosurgeon must make the determination of brain death. We believe that awareness of the clinical features of brain death among PICU physicians should be increased. Secondly, the organ transplantation rates varied between the two hospitals. According to the records of the Ministry of Health, our national donation rate for brain death patients was 23% in 2012[20]. In a Canadian study, the consent rate was 64%[16]. The more informed a family is about the medical condition of the child, the better prepared the family members will be to have a conversation about organ donation[5]. In the study by Tsai et al.[6], multicultural issues were important, with ethnic minorities more likely to refuse consent for donation. The consent rate was 63%; however, only 41% of potential donors proceeded to actual donation, while in another study 47% donated organs[6,16]. In our study, the major reason for a patient's not being an organ transplantation candidate was the family's refusal; this was the case in 15 (75%) of the patients. In some studies, religion, primary language and place of residence were all highly correlated with ethnic background, having an effect on the consent rate[6,21]. In our study, the consent rate for organ donation was 25% when families were approached; 20% of potential donors proceeded to actual donation. We believe that families are significantly more likely to refuse donation due to cultural differences and religious reasons. For instance, in Japan, nearly 30% of the population does not accept brain death as death of the human being; it is thought that the child has a right to live and die peacefully, fully protected against the interests of others[22]. In all instances, families would like to leave the hospital knowing that they had been treated with compassion and respect, just as we would in the case of one of our own family members[3,22-23]. The difference in the donation rates between the two centers in our study may be related to the experience and training of the organ donation coordinator, since Center II has a well-established transplant coordination program. This condition was also reflected in the duration of brain death diagnosis, which was quite significantly different between the centers. Limitations of this study may include its retrospective medical record review design and small sample size.

The PICU physician has an essential role in the diagnosis of brain death and in the organ donation process[6,17,24]. Specialty nurses in the PICU also play a key role in the declaration of brain death, providing the specific clinical information used by the clinician[5]. Decoupling is a process whereby the communication that brain death has occurred is chronologically separated from the request for organ donation to allow time for the parents to accept the brain death of their child[6]. Use of the decoupling process might be useful in causing parents to consider organ donation more favorably, which is important since consent depends mainly on parental willingness. Also, awareness of the need for organs must be promoted through television, films, magazines, handouts, posters in waiting rooms and other means of public communication. This positive interaction would prepare children and adolescents for future decisions that they might have to make concerning family members or their own organs[10,25-26].

Conclusions

There may be potential brain death patients currently waiting to be diagnosed in the intensive care units. We believe that awareness of the clinical features of brain death among PICU physicians should be increased, and that the early diagnosis of brain death and donor organ care are very important issues, especially in children. Prompt evaluation of such patients by ICU physicians once the diagnosis is taken into consideration will probably yield better organs and reduce costs. Increasing children's and adolescents' awareness via means of public communication, as well as additional training of critical care physicians, specialized nurses and organ donation coordinators regarding this subject, may help to increase families' rates of acceptance of organ donation in the future. Further studies with larger samples should be conducted to prevent potential deaths of children on the transplant list.

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