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BRAIN DEATH AND ORGAN DONATION: A LITERATURE REVIEW AND CASE REPORT

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Médico Intensivista pela Associação de Medicina Intensiva Brasileira (AMIB) e Coordenador UTI do Hospital Universitário de Vassouras Vassouras, Rio de Janeiro, Brasil http://lattes.cnpq.br/6616245083862580 Abstract: Brain death in pediatrics is one of the most complex issues in daily practice due to aspects that involve diagnosis, management until the end of life and the possibility of organ donation. The aim of this article is to analyze the subject of brain death and organ donation in pediatrics, based on a case report and to carry out an integrative literature review. Case report and literature review: A 16-year-old patient, hospitalized with a diagnosis of encephalopathy, evolved after 2 months of hospitalization with a seizure disorder and cerebral hemorrhage, which triggered the investigation of brain death. The multidisciplinary UTI team (doctors, nurses, psychology) were involved in the process. Between the first suspicion and the moment of confirmation of death, 1 day elapsed. The entire protocol established by the CFM was followed and the family actively participated in the process, making it possible to obtain organs for transplantation. The review of the topic of brain death and organ harvesting was carried out through an integrative literature review from Scielo and LILACS, with an article insertion date until June 16, 2023, with articles published in English and Portuguese. National legislation on the subject was also analyzed. Pediatric brain death should be managed by a multidisciplinary team, in which there is active family participation and the possibility of organ harvesting as often as possible.

Keywords: organ donation, brain death.

INTRODUCTION

The waiting list for children in need of organ or tissue transplants increases every year, with the constant demand for organs exceeding their supply. This means that some children on the waiting list die before they can undergo a transplant (Eurotransplant International Foundation; American Academy of Pediatrics, Brazil). Many need organs of corresponding size from pediatric donors, especially those awaiting thoracic transplantation. Pediatric donors are predominantly children admitted to a pediatric intensive care unit (PICU) and with an underlying diagnosis of trauma, drowning, cardiac arrest, or neurological disorders.

The first mention of brain death (BD) was made in 1959, mainly observing deep coma, lack of spontaneous breathing and isoelectric electroencephalogram (MOLLARET et al. 1959).

In Brazil, the Federal Council of Medicine (CFM) in 1997 determined to establish the diagnostic criteria for BD and determined that BD would be considered in cases of neurological conditions of known cause and defined as an irreversible process (PRESIDÊNCIA DA REPÚBLICA, 1997). To make this diagnosis, two clinical exams and a complementary exam would be necessary.

The 2017 Decree reinforced that it was up to the CFM to determine the ME criteria (Brazil). Since then, the 2017 CFM Resolution defined ME as the irreversible loss of brain functions, completely, defined by the cessation of electrical activity in the cerebral cortex and brain stem (VILIBOR, 2012).

Considering these aspects, the objective of this article is to analyze the subject of BD and organ donation in pediatrics, based on a case report and to carry out an integrative literature review on BD in pediatrics and organ procurement.

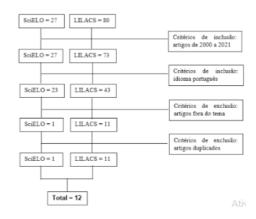
CASE REPORT

16-year-old patient, admitted on 11/06/2020 after reduction of left humeral fracture and suturing of tongue laceration. After a period of 2 months since admission, there was a clinical worsening leading to transfer to the ICU due to the difficult-tocontrol seizure and, later, cerebral hemorrhage, which triggered the investigation of BD. The ICU multidisciplinary team (doctors, nurses, psychology) were involved in the process. Between the first suspicion and the moment of death, 3 days passed. The patient's final moment of life was endured in an environment reserved for the family. We describe a case of ME in a child, with previous neurological impairment, which makes diagnosis difficult. ME in pediatrics is not a common event, even in critical units and must be approached in a multidisciplinary way and involving the family in all stages of the process. On physical examination, the absence of brainstem reflexes was found (absence of cornealpalpebral reflex, absence of the photomotor reflex). In the opinion of neurosurgery, a massive subarachnoid hemorrhage was found. Physical examination was compatible with ME. The EEG trace was slow and slow activity of medium to high voltage was observed with greater projection in frontal regions without defined hemispheric dominance of a non-specific nature. Furthermore, there was a depressed EEG trace, little reactive TCC, hyperdense expansive formation in the cerebellum and occipital region, suggestive of hemorrhage on the head CT with voluminous bleeding in the ENS occupying the cerebellum and occipital lobe region.

LITERATURE REVIEW

An integrative literature review was carried out. The guiding question of the research was: "what is the emphasis in current scientific literature on BD and organ harvesting in pediatrics?" A bibliographical search was carried out in the databases of the Virtual Health Library (VHL), LILACS (Latin American and Caribbean Literature in Health Sciences), Medline and SciELO, using the following descriptors: "brain death", "brain donation", organs", "pediatrics" or "child" or "adolescent" with the Boolean operators "and/ or". The following were used as inclusion criteria for article selection: articles published within the time frame (2000 to 2023) and with an article insertion date up to 06/16/2023, published in English and Portuguese. National legislation on the subject was also analyzed.

In the first phase of the search, a total of 107 articles were found in the databases and after applying the inclusion and exclusion criteria, 1 article remained in SciELO, 11 articles in LILACS, totaling 12 articles, according to the methodology exemplified and presented in **Figure 1**.



The objectives and main results of the 12 articles included in this study, selected based on the descriptors: "brain death" and "organ donation" and "pediatrics" or "child" or "adolescent", are presented in **Table 1**.

IDENTIFICATION AND REFERRAL OF POTENTIAL DONORS

Most articles emphasized the importance of the first step in the donation process: timely identification of potential donors in the PICU and timely referral to an organ procurement organization to increase organ donation rates (Rodrigue JR; American Academy of Pediatrics; Lago). The need for better identification and timely referral of potential donors in neonatal intensive care units (NICU) was highlighted in two articles (Sarnaik AA, Lago). One article studied donation policies after cardiac death in children's hospitals and also studied donors. Most of these hospitals applied clinical indications and restrictions to potential donors, such as not brain dead, dependent, pharmacologically ventilator dependent and imminent death. Minimum ages ranged from 36 weeks of gestational age to 60 months. The minimum weight restriction for newborns was 10 kg.

APPROACH TO PARENTS AND FAMILY

Clear communication must be carried out during the process by the hospital or establishment's care team, which occurs from suspected BD until confirmed death, and must be documented in the medical record. Discussion about organ donation should not occur before the diagnosis of death. It is recommended that the interview with the family regarding organ donation be carried out by a professional with specific training on the subject. The exclusion of life support was already foreseen by the CFM in 2007. Now, both the CFM Resolution of 2017 and the Presidential Decree of 2017, which rectifies the Organ Transplant Law of 1997, define in law the cessation of life support when Organ donation is not viable, at which point the body must be sent for an autopsy or handed over to the family (Novoa, Coelho, Musa).

COLLABORATION WITH ORGAN DONATION ORGANIZATION PROFESSIONALS

Collaboration with professionals from the organ procurement organization during the donation process was considered one of the most relevant topics in most articles, as it increased the chances of successful donation. For example, some authors have recommended early participation of trained professionals in organ procurement organizations, who discuss organ donation, obtain informed consent, and support the family during and after the donation process (Sarnaik). One of the advantages of this early involvement is that the team can help assess the medical suitability of potential donors.

INFORMED CONSENT

The authors of all articles agreed that families must provide consent for certain types of procedures, including pre-death procedures, and must be able to withdraw from the process at any time (Sarnaik).

PALLIATIVE CARE

Palliative care for potential donors and support for the donor's family were key themes in many of the articles. Some authors have specifically focused on the importance of the comfort of potential donors and on specific interventions and therapies to obtain the necessary level of comfort. Others have reported variations in the use of premortem generic medications or procedures in pediatric practice (Navarro). Some premortem procedures may improve the survival of successfully transplanted organs, but they did not specify which procedures (Rabbit).

DEATH DECLARATION

The American Academy of Pediatrics and European Society of Pediatric and Neonatal Intensive Care emphasized that accurate and timely declaration of brain death was essential to ensure successful donation. The neurological criteria for brain death were clearly described: complete loss of consciousness, no spontaneous movement, no reaction to stimuli, no cranial nerve function or reflexes, and no spontaneous breathing during the apnea test. Brain death can be diagnosed in full-term babies from 37 weeks of gestational age (National Health Service).

Resolution CFM 2,173 brought changes to the methodology for diagnosing BD in Brazil, which are highlighted in bold throughout the text in **table 1**.

TEAM EDUCATION

Only a few authors have discussed the specific educational needs of staff for pediatric donation protocols. However, the American Academy of Pediatrics has strongly emphasized the need for regular staff training, which should include medical, ethical, social, cultural, and religious issues related to the potential donor. The Transplantation Society (Rodrigue JR) has specified that training in end-of-life care and organ donation processes must be provided to healthcare professionals of all specializations and disciplines who may be involved in the care of potential or actual donors, not just intensive care professionals. Finally, a study by (Siebelink et al.) that was published in 2012 reviewed the relevant literature and concluded that no education programs for professionals existed at that time.

FINAL CONSIDERATIONS

We describe a case of ME in a child, with previous neurological impairment, which made the diagnosis difficult. ME in pediatrics is not a common event, even in critical units and must be approached in a multidisciplinary way and involving the family in all stages of the process. Health professionals must be sensitive to the entire process involved, so that the family feels welcomed and delicate issues such as organ donation are addressed.

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ANO	AUTOR	OBJETIVOS	RESULTADOS
2008	RODRIGUE ¹	Identify the factors that influence parents' decisions when asked to donate the organs of a deceased child.	Multivariate analyzes showed that organ donation was more likely when the parent was a registered organ donor, the parent had favorable organ donation beliefs, the parent was exposed to organ donation information before the child's death, a limb of the child's health team first mentioned organ donation, the applicant was perceived as sensitive to the family's needs, the family had sufficient time to discuss the donation, and family members agreed on the donation
2015	SARNAIK ²	Evaluate the vital processes of organ donation and transplantation in neonatology and pediatrics and ethical considerations.	The results demonstrate that to maximize the availability of transplantable organs and donation opportunities for terminally ill patients and their families, hospitals must refer potential donors in a timely manner. Prompt investigation and diagnosis of brain death, when applicable, are also crucial, especially in neonates. Empowering individuals from organ procurement organizations to discuss organ donation with families also increased consent rates. Ethical considerations include a potential conflict of interest between the dying patient and others who may benefit from the organs, and the accuracy of the donor's declaration of death.
2012	SIEBELINK ³	Identify donor identification, parental consent and completion rates, as well as adherence to the national protocol.	The parental consent and compliance rate was 42%. Sixty-three (48%) potential tissue donors were correctly identified; the parental consent and compliance rate was 27%. Correct identification increased with age (logistic regression, organs: $P = 0.024$; tissues: $P = 0.011$). Although an 84% overall identification rate of potential organ donors may seem acceptable, the observed variation suggests room for improvement, as does the low overall identification rate of pediatric tissue donors.
2010	AMERICAN ACADEMY OF PEDIA- TRICS ¹	Analyze the significant benefit to prolong the lives of young recipients of these organs and a high emotional impact on the families of donors and recipients.	It was noted that efforts are needed from pediatric professionals to shape public policies to provide a system in which procurement, distribution and cost are fair and equitable for children and adults. The main issues of concern are the availability of and access to donor organs; process supervision and control; pediatric medical and surgical consultation and ongoing care throughout the organ donation and transplant process; ethical, social, financial and monitoring issues; insurance coverage issues; and public awareness about the need for organ donors of all ages.
2014	NATIONAL HEALTH SERVICE ⁵	Estimate pediatric organ donation statistics in the United Kingdom.	It was found that the reason for the increase in donation from young children has been attributed to the advances and development of en bloc kidney transplantation techniques, the development of hepatocyte transplantation in this age group and media coverage that has allowed families to feel empowered to seek information about the organ donation option.
2007	LAGO ⁶	To evaluate the incidence of brain death, as well as the conduct and protocols adopted after diagnostic confirmation in seven pediatric intensive care units (PICU) located in three Brazilian regions.	The most frequent cause was intracranial hemorrhage (31.1%). In 80% of cases, the clinical diagnosis of BD was confirmed by complementary examination (100% in the South Region, 68% in the Southeast and 72% in the Northeast, $p = 0.02$). The withdrawal of life support after a diagnosis of BD differed in the three regions, being faster ($p = 0.04$) in the South (1.8±1.9 h) than in the Southeast (28.6±43.2 h) and Northeast (15.5±17.1 h). Only six (9.8%) children with BD were organ donors. Although the law that defines criteria for ME has existed in Brazil since 1997, we found that it is not uniformly followed. Consequently, unnecessary vital support is offered to individuals who have already died, and there is still a modest involvement of PICUs with organ donations.
2020	MUSA ⁷	To evaluate the knowledge of students from Undergraduate Nursing, Psychology and Social Work courses on the concept of Brain Death and aspects of the organ and tissue donation and transplantation process.	449 academics participated in the study. It was found that the participants have knowledge about the process of organ donation and transplantation, but with gaps, which reflect the importance of these future professionals seeking to deepen their knowledge on this topic. It is important to highlight the importance of healthcare professionals knowing the donation and transplantation process, which can contribute to increasing the number of donations.

2014	RODRIGUES ⁸	Characterize the profile of effective organ and tissue donors in addition to knowing which organs and tissues were donated for transplants.	It was evident that there was a predominance of white individuals (72%), males (55%), aged between 41 and 60 years (44%), with the main cause of brain death being stroke (55%). Regarding antecedents, 31% were classified as overweight, followed by systemic arterial hypertension (27%) and diabetes mellitus found in only 4.3% of donors. The use of vasoactive drugs was present in 92.7% of donors, and the main drug used was noradrenaline (81.6%). Hyperglycemia and hypernatremia were found in 78% and 71% of donors, respectively.
2007	NAVARRO ⁹	Investigate deceased donor organ transplant programs and their complex structure from a medical, logistical and cultural point of view.	The results revealed that 71.42% of donors and 64.15% of non- donors had medico-legal implications. The main cause of death and brain injury was traumatic brain injury (66.97%). The donor rate per million inhabitants was 8.3. It was found that adequate management of medico-legal aspects influences the deceased donor rate achieved. This, together with the coordination and implementation of the Transplant Council, made it possible to obtain the highest donation rate of this type in the country.
2007	COELHO ¹⁰	Determine the opinion and knowledge of a sample of the population of the city of Curitiba about organ donation and transplantation.	It was found that the majority of respondents (87.8%) were in favor of organ donation. There was no difference in the percentage of the population in favor of organ donation in relation to sex, marital status, religion and income. The main reasons for being in favor of organ donation were to save lives, help others and donate life. The main reasons for not being in favor of donation were a lack of trust in medicine or in the system for collecting and distributing organs, because there is a trade in organs and fear of mutilation of the body. The majority of those interviewed responded that the rich were more likely to be transplanted than the poor, that organs are sold in Brazil and that there is a possibility of an error in the diagnosis of brain death established by the doctor. The majority of the population in this study is in favor of organ donation and has good knowledge about organ donation and transplantation. The majority demonstrated that they did not trust the organ distribution system and the diagnosis of brain death.
2005	PEREZ ¹¹	Present a discussion on four aspects of the legislation and medical ethics of transplants: the concept of death, organ donation, the selection of recipients and the future of therapeutic transplants.	It was noticed that after the diagnosis of brain death, the two legal and ethical forms of organ donors, the most frequent criteria and problems for the selection of recipients and the nature of the medical technology transition of therapeutic transplants are the biggest impasse for the formation of a universal law.
2007	NOVOA ¹²	Understand the legislation and review and ethical analysis of brain death.	It was found that the diagnosis of brain death is considered in the Western world as a new way of being dead. This concept, in our country, is not fully incorporated both in the general population and in the healthcare team. In our experience, a significant percentage of pediatric providers consider that a brain-dead child has not died. Given this situation, it is estimated that training should be carried out in services in this condition and allow professionals who do not accept brain death as equivalent to the death of the individual to not be involved in decisions made with these children.

Quadro 1- Brain Death.

The participation of the neurologist is not mandatory		
Doctors must be trained to diagnose ME		
Determination of a minimum duration of observation and treatment before initiating ME determination		
Compliance with physiological prerequisites for the diagnosis of ME		
Reduction of the time interval between the two clinical examinations		
Possibility of clinical examination in cases of unilateral anatomical lesion of the eyes or ears		
Performance of a single apnea test		

Pre-test blood gas analysis, ideally with PaO 2 \geq 200mmHg and PaCO 2 between 35 and 45mmHg

Possibility of carrying out an apnea test using CPAP

Adequate communication with family members before and throughout the ME diagnosis process

Interruption of life support when organ donation is not feasible

New ME Determination Declaration to be completed by all doctors involved in the diagnosis.

Procedures should be initiated when BD is suspected in those with deep coma, lack of supraspinal reflexes and persistent apnea, according to Table 1.

A. Communicating suspected ME to relatives

- Relatives must be informed about suspected brain death and the steps to determine it.

- Family members must receive updated information at each stage of the ME determination process.

B. ME notification

- Notify the State Transplant Center that the BD determination has started

C. Prerequisites to be met at the beginning and during the ME determination procedure

- Presence of brain injury of known cause, irreversible and capable of causing ME.

- Absence of treatable factors that may confuse the diagnosis of ME (e.g. sedatives)

- Treatment and observation in hospital for a minimum period of 6 hours. This period of observation and treatment must be at least 24 hours in cases of hypoxic-ischemic encephalopathy or after the rewarming phase of therapeutic hypothermia

- Body temperature > 35°C, SatO 2 > 94% and blood pressure according to age group:

Age group	SBP (mmHg)	PAM (mmHg)	
\geq 16 anos	100	65	
7 - 16 anos não inclusivo	90	65	
2 - 7 anos não inclusivo	85	62	
5 meses - 2 anos não inclusivo	80	60	
Até 5 meses não inclusivo	60	43	

D. Two clinical tests that detect signs compatible with TB

- Eat deep

- Absence of brain stem reflexes	
pupillary light	
cornea-palpebral	
oculocephalic	
vestibulo-ocular	
cough	

Time	Minimum time interval between the two exams
7 full days (full-term baby) up to 2 months	24 hours
2 - 24 months not inclusive	12 hours
Over 2 years old	1 hour

E. Apnea test

- Lack of spontaneous respiratory movements after interruption of ventilation during maximal stimulation of the respiratory center with documentation of PaCO 2 > 55 mmHg

- F. Complementary tests
- Electroencephalogram
- Cerebral angiography
- Transcranial Doppler
- Brain scintigraphy

G. Management after determination of brain death

- Mandatory notification of ME to the State Transplant Center

- Completion of the death certificate. If death is due to an external cause, it must be completed by the coroner

- Report the death to family members as soon as it is determined
- Any mention of organ donation should only occur after the death is reported
- Withdrawal of life support in cases where organ donation is not viable

Table 1 – Determination of Brain Death.