Review Article

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Diagnosis and Declaration of Death: A Dilemma

Niranjan Kumar Verma[1], Ashutosh Ranjan[2], Alok Kumar Singh[3]

[1]Professor and Head, Department of Anaesthesiology and Critical Care, JLN Medical College, Bhagalpur, Bihar, India, [2]Senior Resident, Department of Anaesthesiology and Critical Care, JLN Medical College, Bhagalpur, Bihar, India, [3]Assistant Professor, Department of Anaesthesiology and Critical Care, JLN Medical College, Bhagalpur, Bihar, India

Abstract

Diagnosis and thereby declaration of death are one of the important duties of a clinician. Development in the field of advanced resuscitation techniques together with the benefits and need for cadaveric organ donation has made the need for scientific and correct diagnosis of brain deaths; where the brain stem is irreversibly damaged but heart is still beating and body is kept alive by ventilator, so as to make organ donation feasible. In the review we have tried to elaborate it in completeness. We have here tried to summarize the different accepted guidelines for clear cut diagnosis of brain death, such as to make it more precisely

Key words: Apnea testing, Asystolic donors, Brain death, Cadaveric organ donation, Cardiopulmonary resuscitation, Heart beating brain dead donors

INTRODUCTION

The diagnosis, confirmation, and certification of death are the vital necessary skills for any medical professional, especially those who are attached with big institutions and intensive care unit. Although confirmation of death is straightforward in the majority of cases, development in the field of advanced resuscitation techniques together with the need and benefits of cadaveric organ donation presents the clinicians working in the advanced center with the specific challenge to understand the essential distinctions between what is alive and what is dead. We have here tried to summarize the different accepted guidelines for clear cut diagnosis of brain death, such as to make it more precisely.

HISTORICAL PROSPECTS

A history is full of examples of failure to distinguish deep coma from death and phrases like, "graveyard shift" has emerged. The effectiveness of cardiopulmonary resuscitation in maintaining cerebral perfusion has challenged the concept that cardiac arrest is irreversible associated with death. Similarly, intervention in patients with terminal respiratory arrest secondary to an intracranial catastrophe has led to the emergence of a state of profound and irreversible apneic coma in patients whose heart continue to beat for as long as mechanical ventilation is continued. This second group of patients has led to the emergence of widely accepted criteria of brain death. Now, the key elements of brain death are irreversible loss of capacity to breathe, combined with the irreversible loss of capacity for consciousness.[1,2] Hence, death has been divided into two groups: Brain death and cardiopulmonary or somatic death. To distinguish between the two is important as outcomes of transplantation from organs retrieved from "Heart beating brain dead donors are considered superior to those from asystolic donors." Hence, nowadays, brain death has become inextricably linked with organ donations.

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FUNDAMENTAL CONCEPT OF DEATH

The possibility of successful resuscitation in a patient who has recently suffered a cardiac arrest together with the maintained circulation and somatic physiology in an individual, who is brainstem dead, highlights the inadequacy of using only the cardio-respiratory criteria in the diagnosis of death. The diagnosis of death by cardio-respiratory criteria can be done with confirmation if there is continuous asystole for more than 5 min duration. This should be done by continuous electrocardiogram and intra-

Corresponding Author: Dr. Niranjan Kumar Verma, Mayaganj Doctor's Colony, Opposite JLN Medical College and Hospital, Bhagalpur - 812 001, Bihar, India. Phone: +91-9431257415. E-mail: nkverma2001@gmail.com

arterial pressure monitoring and/or an echocardiography examination.[3] If there is return of signs of any cardiac or respiratory activity within this 5 min period, the check should be continued for another 5 min asystole period. At least two different sets of clinician, one of them being a neurologist or an anesthesiologist should confirm the diagnosis before the declaration of death.

Practical parameters for determining brain death in adults:[4,5]

A. Prerequisites: Brain death is the absence of clinical brain function when the proximate cause is unknown and demonstrable irreversible.
   1. Clinical or neuroimaging evidence of an acute central nervous system (CNS) catastrophe that is compatible with the clinical diagnosis of brain death
   2. Exclusion of complicating medical conditions that may confound clinical assessment 9 no severe electrolyte, acid-base, or endocrine disturbance)
   3. No drug intoxication or poisoning
   4. Core temperature ≥32°C.

B. The three cardinal findings in brain death are coma or unresponsiveness, the absence of brainstem reflexes, and apnea.
   1. Coma or unresponsiveness - no cerebral motor response to pain in all extremities (nail bed pressure and supraorbital pressure).
   2. The absence of brainstem reflex.
      a. Pupil
         i. No response to bright light
         ii. Size: Mid position (4 mm) to dilated (8 mm).
      b. Ocular movement
         i. No oculocephalic reflex 9 tested only when no fracture or instability of cervical spine is apparent)
         ii. No deviation of eyes to irrigation of each ear with 50 ml of cold water (allow 1 min after injection and at least 5 min between testing of each ear).
      c. Facial sensation and facial motor response
         i. No corneal reflex to touch with a cotton swab
         ii. No jaw reflex
         iii. No grimacing to deep pressure on nail bed, supraorbital ridge or temporomandibular joint.
      d. Pharyngeal and tracheal reflexes
         i. No response after stimulation of posterior pharyngeal wall with tongue depressure
         ii. No cough response to bronchial suction.
   3. Apnea testing performed as follows:
      a. Prerequisites
         i. Core temperature ≥36.5°C
         ii. Systolic blood pressure ≥90 mm Hg
         iii. Euvolumia-positive fluid balance in the previous 6 h
         iv. Normal $PaCO_2$-arterial $PaCO_2$ ≥40 mm Hg
         v. Normal PaO_2-pre-oxygenation to obtain arterial PaO_2 ≥200 mm Hg.
      b. Connect a pulse oximeter and disconnect the ventilator.
      c. Deliver 100% O_2, 6 L/min, into the trachea by placing a cannula at the level of the carina.
      d. Look closely for respiratory movements (abdominal or chest rising).
      e. Measure arterial PaO_2, PCO_2, and pH after approximately 8 min and reconnect the ventilator.
      f. If respiratory movements are absent and arterial PCO_2 is ≥60 mm Hg, the apnea test result is positive supporting the diagnosis of brain death.
      g. If respiratory movements are observed, the apnea test result is negative, suggesting no death as yet.
      h. Connect the ventilator if, during testing, the systolic blood pressure becomes ≥90 mm Hg or the pulse oximeter indicates significant oxygen desaturation and cardiac arrhythmias are present; immediately draw an arterial blood sample and analyze arterial blood gas. If PCO_2 is ≥60 mm Hg or PCO_2 increase is ≥20 mm Hg over baseline normal PCO_2, the apnea test result is positive (it supports the clinical diagnosis of brain death); if PCO_2 is ≤60 mm Hg or PCO_2 increase is ≤20 mm Hg over baseline normal PCO_2, the result is intermediate, and an additional confirmatory test can be considered.

Drug Intoxication

Drug intoxication represents a clinically significant reversible cause of coma and may complicate assessment on occasions where the patient has received an infusion of sedative drugs as part of their critical care treatment and when their brain injury is drug induced.[6] The most problematic of circumstances are those where drug elimination is impaired by reduced hepatorenal function, or where agents with long half-lives have been used. A possible approach should be as follow:

a. A period of observation of four times the elimination half-life of the agent involved to allow effective drug elimination. This approach is best suited to circumstances where short-acting agents like propofol and alfentanil have been given to patients with normal hepato-renal functions.
b. The administration of specific antagonists such as flumazenil or naloxone in circumstances where the residual effects of opioids or benzodiazepines are required.
c. Plasma analysis to confirm that a suspected sedative

is either not detected or at a sub-theraputic level. This opinion is particularly suited for agents with long or unpredictable half-lives, such as thiopental or phenobarbital.

d. A confirmatory test to demonstrate the absence of cerebral blood flow or perfusion, as cerebral angiography.
e. Despite this general guidance, the revised Academy of Medical Royal College Code remains permissive and give a clinician the liberty to dismiss the influence of sedative drugs in circumstances where there is independent evidence to suggest that the patient is brainstem dead as suggested by computed tomography of head or a prolonged period of malignant intracranial hypertension.
f. Other causes of apnea as some neuromuscular weakness from any cause, cervical spinal cord injury which causes respiratory paralysis. A nerve stimulator is used routinely to confirm the absence of residual drug related neuromuscular block.
g. Hypothalamic and anterior pituitary functions may be preserved to some extent for a certain period of times after the onset of brain death. The response of the immune system to stimulation is modified considerably after total and irreversible loss of CNS function.

Pitfalls in the Diagnosis of Brain Death

The following conditions can interfere with the clinical diagnosis of brain death so that the diagnosis cannot be made with certainty on clinical grounds alone. In such cases, confirmatory tests are recommended.

1. Severe facial trauma
2. Pre-existing pupillary abnormalities
3. The toxic level of any sedative drugs, aminoglycosides, tricyclic antidepressants, anticholinergics, antiepileptic drugs, chemotherapeutic agents, or neuromuscular blocking agents 16
4. Sleep apnea or severe pulmonary diseases resulting in chronic retention of CO_2.

Clinical Observations Still Compatible with the Diagnosis of Brain Death

These manifestations are seen occasionally and should not be misinterpreted as evidence of normal brainstem function.

1. Spontaneous spinal movements of limbs (not to be confused with pathological flexion or extension response)[7-9]
2. Respiration like movements (shoulder elevation and adduction, back arching, intercostal expansion without significant tidal volume
3. Sweating, blushing or tachycardia
4. Normal blood pressure in the absence of pharmacological support
5. The absence of diabetes in sipidus (normal osmolar control mechanism)
6. Deep tendon reflexes, triple flexion responses or Babinski's reflex.[10,11]

Confirmatory Laboratory Tests Supporting the Diagnosis of Brain Death

Brain death is a clinical diagnosis. Hence, repeat clinical evaluation after about 6 h. A confirmatory test is not mandatory but can be used as supportive data in which specific components of clinical testings cannot be reliably performed or evaluated. Remember to write down the names of the physicians interpreting the ancillary tests, as this will be needed in the declaration of death note.

1. Conventional angiography: No intracerebral filling at the level of the carotid bifurcation or circle of Willis is observed. The external carotid circulation is present, and filling of superior sagittal sinus may be delayed.[12]
2. Electroencephalography-no electrocerebral activity is present during at least 30 min of recording that adheres to the minimal technical criteria for electroencephalogram (EEG) recording in suspected brain death as adopted by American encephalographic society, including 16 channels EEG. It should include the absence of non-artefactual activities and no change should appear with auditory, visual or painful stimulation. Electrocardiographic artifact should be visible. No need is seen for the patient to be normothermic, but core body temperature should be above 90*F. If an EEG is obtained, the absence of EEG activity should be confirmed by a neurologist before the declaration of brain death. This should be noted in the patient's medical record.[13,14]
3. Transcranial Doppler ultrasonography:[15]
    a. Small systolic peaks in early systole occurring without diastolic flow or with the reverberating flow are indicative of very high vascular resistance associated with greatly increased intracranial pressure and lack of tissue blood flow.
    b. Previously documented Doppler signals are lost, because 10% of patients may not have temporal window that permits insonation, however, the initial absence of Doppler signals cannot be interpreted as consistent with brain death.
    c. Technetium-99-hexamethylpropyleneamineoxime brain scan; No uptake of isotope in brain parenchyma (hollow skull phenomenon) occurs, as interpreted by a nuclear medicine physician.
    d. Somatosensory evoked potentials: The N20-P22 response with median nerve stimulation is absent bilaterally. The recording should adhere to the minimal technical criteria for somatosensory evoked potentials recording in suspected brain

death as adopted by American encephalographic society.

Diagnosis of Brainstem Death in Children

Brainstem death is diagnosed in the same way in children of more than 2 months old. Diagnosis is made by two clinicians among whom one must be a pediatrician. In infants younger than 2 months of age, the diagnosis of brainstem death becomes difficult. Coma in this age group is often multifactorial. Although hypoxic encephalopathy remains the most likely cause of massive brain injury. It is often difficult to demonstrate structural brain damage, and thus, the preconditions are rarely met. In preterm infants of gestational age below 37 weeks, there is little evidence regarding normal brainstem reflexes and as such their absence is difficult to demonstrate, and thus, the diagnosis of brainstem death is inappropriate. There are certain guidelines for brain death in children.[16-18]

A. History: Consider the cause of coma so as to eliminate reversible and remediable conditions
B. Criteria for physical examinations
    1. Coma and apnea.
    2. The absence of brainstem functions.
        a. Fully dilated pupil
        b. Absence of caloric-induced eye movement
        c. Absence of bulbar musculature, corneal, gag, sucking, and rooting reflexes
        d. Absence of respiratory effort with standardized Apnea testing.
    3. There should be no hypotension or hypothermia
    4. Flaccid tone and absence of spontaneous or induced movements excluding activities initiated at spinal cord level
    5. The examination should remain consistent throughout the predetermined observation period.
C. Observation period according to age:
    1. 7 days to 2 months age: Two examinations and EEGs, 48 h apart.
    2. 2 months to 1 year age: Two examinations and EEG 24 h apart and/or one examination and an initial EEG showing elecrocerebral silence combined with a radionuclide angiogram showing absence of cerebral blood flow.
    3. Over 1 year age: Two examinations 12 and 24 h apart and EEG.

Although the guidelines are exhaustive, there are several fallacies:

1. In case of intrauterine injury, the duration of assault and its severity may be difficult to establish
2. Normal systemic arterial pressure is difficult to determine
3. The EEG and transcranial Doppler sonography may not be 100% reliable
4. The clinical examinations cannot be reliable due to immaturity.[17]

CONCLUSION

Diagnosis and thereby declaration of death are one of the important duties of a clinician. Social, professional, and sometimes legal complications are reported due to a misdiagnosed death. Hence, it should be carried out patiently and with proper documentations. Death consists of the loss of capacity for consciousness and the loss of the ability to breathe. Brainstem death occurs after neurological injury when the brain stem has been irreversibly damaged, but the heart is still beating and body is kept alive by a ventilator. Always two appropriately qualified clinicians are required to diagnose a brainstem death after exclusion of reversible cause of unconsciousness, confirmation of the absence of brainstem reflexes and completion of apnea testing. Cardiorespiratory death can be diagnosed after 5 min of observed asystole, long enough for irreversible damage to the brain stem to have occurred.

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