Bilan N., et al., ***J Anal Res Clin Med,*** 2014, 2(2), 53-6.
doi: 10.5681/jarcm.2014.009

Original Article

Apnea testing: A simple prognostic test for diagnosis of brain-death

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Article info
Article History:
Received: 24 Jan. 2014
Accepted: 20 Mar. 2014

Keywords:
Apnea Testing,
Brain-Death,
Pediatrics

Abstract

Introduction: Brain-death is the end stage of most illnesses that cause brain injury and decrease oxygenation and circulation of brain tissues. Early determination of brain-death is essential to the prevention of expensive modeling in the pediatric intensive care unit (PICU) and reserving facilities for patients with good prognosis. Apnea test is one of the important brain-death determining methods in clinical evaluation that can be performed easier and faster than other methods.

Methods: In a cross-sectional study, 75 patients with brain-death criteria were evaluated from 2003-2011. Apnea testing was fulfilled through standard methods. Patients who did not develop spontaneous respiration at $PaCo_2$ level of 60 mmHg or more were confirmed as brain-dead.

Results: Mean age of patients was 40 months. All patients were comatose, without brainstem reflexes. Cause of coma was status epilepticus in most patients. All patients that had a positive apnea test died after a mean duration of 8 days.

Conclusion: All other confirmative methods, irrespective of their accuracy, need complex instruments and experienced manpower, and are expensive which makes their preparation impossible in most ICU centers. However, apnea test is a simple prognostic method in brain-death confirmation with 100% accuracy.

Citation: Bilan N, Ghalehgolab-Behbahan A, Shiva Sh. **Apnea testing: A simple prognostic test for diagnosis of brain-death.** J Anal Res Clin Med 2014; 2(2): 53-6.

Introduction

Brain death is the simultaneous and irreversible loss of all cortical, subcortical, and brainstem functions and is defined as a specific clinical and paraclinical condition.[1] It could be the end stage of most illnesses that cause brain injury and decrease oxygenation and circulation of brain tissues.

In 1987, guidelines for pediatric brain-death determination were published by a multi-society task force that emphasized the importance of medical history and clinical examination to eliminate reversible conditions.[2] The early determination of brain-death is essential to the prevention of expensive modeling in pediatric intensive care unit (PICU) and reserving facilities for patients with good prognosis. On the other hand, deciding to stop supportive therapy in very ill patients is challenging. Therefore, it is essential for all critical care units to establish a process for determining brain-death.[3] Diagnosis of brain-death is primarily clinical.[1] Different processes, including Electroencephalography (EEG), cerebral angiography, and auditory brainstem evoked potential, were established

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for diagnosis, but they are expensive and are not available in some clinics. Apnea test is one of the important determining methods in clinical evaluation of brain-death that can be performed easier and faster than others.[4,5] Mathur et al. have evaluated variability in pediatric brain-death determination in California and shown that apnea testing, despite its volubility, is documented in less than 50% of the patients, and only one third of them have sufficient increase in $PaCO_2$ during the test. Therefore, most apnea tests were performed with inadequate increase in $PaCO_2$.[6]

As in Guidelines for the Determination of Brain-Death in Infants and Children, apnea testing should be performed for brain-death confirmation in each neurologic examination for all patients unless a medical contraindication exists. If apnea testing cannot be completed safely, an ancillary study should be performed to assist with the determination of brain-death.[2]

Methods

In a cross-sectional study, 75 patients with brain-death criteria were evaluated from 2003-2011.

Inclusion criteria were:

A) The history of potential cause of brain-death with irreversible and untreatable conditions:

1) Absence of CNS suppressing and neuromuscular blocking drugs; if it present, discontinued for a long enough time period before evaluation assessed by toxicology screen or serum levels

2) Absence of metabolic or toxic abnormality

3) Absence of electrolyte abnormality or endocrine disorder

4) Absence of hypothermia (core temperature < 32 ^{o}C)

5) Absence of circulating abnormality (especially hypotension)

B) Confirmed brain-death in clinical evaluation:

1) Coexistence of coma and apnea

2) Complete absence of consciousness and spontaneous movements

3) Absence of brainstem reflexes:

a) Pupils are fixed in a midsize or dilated position without response to light

b) Absence of ocular movements: spontaneous, oculovestibular, and oculocaloric movement

c) Absence of oropharyngeal and facial movements

d) Absence of corneal, gag, coughing, sacking, and rooting reflexes (not including withdrawal spinal reflexes)

e) There was an observation period that varied based on patients' age, during that period clinical examination must be unchanged and confirm the diagnosis of brain-death. Recommended observation periods are 48 hours for 7 days to 2 months, 24 hours for 2 months to 1 year, and 12 hours for older patients.

All patients were evaluated by a pediatric neurologist according to the above criteria.

While patient was under mechanical ventilation an arterial blood gases (ABGs) were performed to determine $PaCo_2$, and maintain $PaCO_2$ level at normal range. After pre-oxygenation with 100% oxygen for at least 10 minutes, respiratory supports were withheld. Then, 100% FiO_2 was supplied with CPAP mode for a period long enough to achieve a $PaCo_2 \geq 60$ mmHg (10 minutes or more), then the test was stopped and mechanical ventilation was continued.[1,7-18] During the test the patients were evaluated carefully and pulse oxymetry, cardiac monitoring, and blood pressure were controlled.

Those who did not develop spontaneous respiration at $PaCo_2$ level of 60 mmHg were confirmed brain-dead.

Apnea testing cannot be performed in these circumstances:

1- Patients with cervical spinal cord injuries

2- Patients with severe acute lung injuries

3- Patients undergoing high-frequency oscillatory ventilation

4- Patients who develop oxygen desaturation because of an underlying lung injury

5- Patients with hypotension resulting from

hypercarbia causing respiratory acidosis.[6]

Results

Mean age of patients was 40 months (3 months to 6 years, 17 male and 13 female, and serum sodium concentration was between 136-150, 29 normal temperatures and 1 febrile patient).

In neurological examination all patients were comatose, with apnea and mydriatic pupils without response to light, and no brainstem reflexes. In addition, 6 patients showed spinal withdrawal reflexes in response to painful stimulants. Moreover, 2 patients exhibited extensor plantar reflex.

Causes of coma were status epilepticus in 50 patients (66.6%), neurologic disorder in 15 patients (20.0%), and septic shock in 10 patients (13.3%). Mean duration of PICU hospitalization was 8 days (5-11 days).

The apnea test was positive in all patients and confirmed the diagnosis. Checking ABG, mean PaO_2 was 105.6 mmHg before and 39.3 mmHg after the apnea test. In addition, mean $PaCO_2$ was 97.3 and 115.3 mmHg before and after the apnea test, respectively.

Discussion

Early diagnosis of brain-death in PICU is important due to:

1) Treatment and supportive care after brain-death were ineffective and did not change patient's outcome, and sometimes even put the families in stressful situations and imposed treatment expense on the family.

2) Occupying of PICU beds by poor prognosis patients deprives patients with better prognosis of them and forfeits facilities.

3) Long duration of hospitalization increases the rate of infectious disease and other complications in patients and thus affects organ transplantation.

In this study, most patients were unstable, due to shock, hypotension, electrolyte disturbance, anticonvulsant, central nervous system (CNS) suppressant drugs, and etcetera, at admission that prevented the performance of apnea test on the first days. Therefore, we needed a few days to stabilize the patients, correct electrolyte disturbances, and discontinue sedative drugs. Determination of serum drug levels does not affect brain-death confirmation.[5]

In some studies, during apnea test patients were disconnected from the ventilator and supplied with 6 lit/min oxygen with an intratracheal catheter. In this method, displacement of catheter and predisposing pulmonary disease result in hypoxia and discontinuation of the test.[7,8,9] Furthermore, Co_2 depletion through oxygen flow defers $PaCo_2$ increasing, prolongs test duration, and induces complications.[13] Instead of an intratracheal catheter we used continuous positive airway pressure (CPAP) with 100% FIO_2, 8 lit/min flow rate, and 5-7 cmH_2O pressure. During the standard time duration of 10 minutes or more, mean $PaCo_2$ increased from 39.3 to 115.5; this was far more than the apnea test confirmation. In the case of the development of each of the following results, the test was stopped: hypotension; heart arrhythmia; and hypoxia (O_2 saturation < 90% in pulse oximetry).

Other confirmative tests for brain-death include:

1) EEG: The absence of brain electrical activity of more than 2 microvolts during 30 minutes of EEG recording in comatose patients, through electrodes with 10 cm distance from each other is named electro cerebral silence (ECS). If 2 EEGs separated by 24 hours were recorded and both of them had ECS, brain-death diagnosis was confirmed. EEG is not available in all hospitals and has false positive and false negative results.[5,19-21]

2) Brain stem auditory evoked potentials

3) Cerebral blood flow evaluation:

a) Cerebral radionuclide scanning

b) Intracranial 4 vessel cerebral angiography

c) Common carotid pulsed Doppler ultrasound

d) MRI with phosphorus 31

e) PET scan: It is not recommended in brain-death confirmation, because it reports inflammatory cell secretion in the brain as

glucose metabolism.[5]

All of these methods, irrespective of their accuracy, need complex instruments and experienced manpower, and are expensive, which makes their preparation impossible in most ICU centers.

Conclusion

Apnea test is a simple, inexpensive, quick, and feasible method with 100% accuracy in brain-death confirmation.

Conflict of Interests

Authors have no conflict of interest.

Acknowledgments

We would like to thank the Tuberculosis and Pulmonary Disease Center for their advances.

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