Confirmation of Brain Death Using Brain Radionuclide Perfusion Imaging Technique

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Key Words

Brain death · Brain radionuclide perfusion · Kuwait

Abstract

Objective: To determine the reliability of radionuclide cerebral blood perfusion imaging in confirming brain death irrespective of continued heartbeat. **Subjects and Methods:** Twenty-eight patients (19 male and 9 female, aged 17–63 years) with severe brain injury and fully supported until the final cardiac asystole were included in the study. Two sets of clinical tests aimed at ascertaining brain death in each subject were performed separately for each case within an interval of 24 h. Dynamic, planar and single photon emission computed tomographic (SPECT) brain scintigraphy were also performed after intravenous administration of 550 MBq (15 mCi) technetium-99m hexamethyl propyleneamine oxime. **Results:** Following the clinical diagnosis of brain death, none of the patients was withdrawn from cardiopulmonary support or had any organ harvested. Dynamic, planar and SPECT imaging performed thereafter did not reveal any intracranial cerebral perfusion in any of the subjects, except in 1 patient where the initial scan showed posterior fossa activity that ceased, in a subsequent scan obtained after 24 h. All of the patients were declared

dead only after the emergence of cardiac asystole. **Conclusion:** The findings indicate that radionuclide brain perfusion imaging is reliable, reproducible, noninvasive and simple to perform for the confirmation of brain death and as such we recommend it as an alternative to exhaustive neurophysiological tests and invasive catheter angiography.

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Introduction

In most Western societies a consensus has evolved over the last three decades that when test requirements for brain death are satisfied, the patient can be declared medically and legally dead, irrespective of continued heartbeat [1–4]. Upon the diagnosis of brain death, when respiratory and other supportive techniques are stopped, the heart stops beating within hours to a few days. This concept of brain death is however still not widely accepted or applied in many countries and societies. In Kuwait, as in most Islamic countries, cessation of cardiac function is the usual criterion for declaration of death, despite the acceptance of brain death by the majority of Islamic jurists at their meeting held in Amman, Jordan, in 1986 [5]. In these countries, in almost all cases the society has

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Fig. 1. Planar (**a**) and SPECT (**b**) images showing normal cerebral perfusion in supratentorial and infratentorial cerebral compartments.

not accepted brain death criteria as sufficient evidence to discontinue supportive care, primarily due to slow cultural acceptance of the concept of brain death. Futile treatment may therefore be continued, consequently slowing down and hindering the procurement of vital organs for transplantation, the demand for which is on the increase. Hence, we decided to prospectively study the reliability and reproducibility of the application of radionuclide brain perfusion imaging technique in confirming the standardized and widely accepted test batteries in the clinical bedside determination of brain death in Kuwait.

Subjects and Methods

We prospectively examined 28 patients (19 male and 9 female) aged 30.5 ± 11.7 years (range 17–63) who were admitted to Al-Amiri and Mubarak Al-Kabir Hospitals, Kuwait (two major tertiary care centers affiliated with the Faculty of Medicine, Kuwait University, Kuwait) over a period of 11 years (1992–2001). All of the patients

had a devastating brain injury (sufficient to lead to irreversible coma) and as such were suspected to be brain-dead. None of them was a potential organ donor. All the patients received the same standard medical care, including ventilator care and full medical support, and all also had CT scanning of the brain. In no case was supportive treatment withheld because of the presence of signs of brain death. After establishing the usual clinical criteria of brain death, that included absence of cerebral, brainstem and unsupported respiratory functions, radionuclide brain perfusion studies (dynamic, planar and single photon emission computed tomography, SPECT) were performed.

A 5-ml volume of freshly eluted technetium-99m pertechnetate was used to prepare technetium-99m hexamethyl propyleneamine oxime (^{99m}Tc -HMPAO) according to recommendations of the manufacturer (Amersham International PLC, UK). Thin-layer chromatography was done to determine the radiopharmaceutical purity prior to injection. The ^{99m}Tc -HMPAO was injected within 30 min of preparation by a physician, who selected the most possible central access.

Dynamic images (1 s/frame for 60 s) were acquired, followed by planar static images (anterior, posterior, lateral and vertex views each for 5 min) and SPECT (64 projections on single-head ZLC Digitrac camera, Siemens, Erlangen, Germany, each projection for 20 s). The SPECT images were reconstructed using BW 0.55/7 filter and filter

back-projection technique. One-pixel-thick slices (about 11 mm) were displayed along with dynamic and static images. Gray and color scales were used to display images on the screen for visual interpretation. The entire procedure lasted about 60 min. Brain death was reported using the combined criteria: absent flow on dynamic study; nonvisualization of sagittal sinus; no uptake of the radiotracer within the brain regions on both planar and SPECT images.

Results

The demographic data and the etiology of brain death are listed in table 1. Head injury and intracerebral hemorrhage were the most frequent causes of death, each occurring in 10 patients. Other causes were cerebral infarcts in 3 patients, anoxic encephalopathy also in 3 patients, brain tumor and drug overdose, each in 1 patient. All patients were declared brain-dead after satisfying the standard clinical criteria, performed twice at an interval of 24 h.

A normal cerebral blood perfusion image is shown in figure 1, while that of brain death is shown in figure 2. In the 28 patients, no cerebral blood flow in dynamic, planar or SPECT imaging was detected supratentorially and

Table 1. Demographic data and diagnosis of the patients

Patients	Sex	Age		Diagnosis
		mean $\pm$ SD	range	
10	all male	24.2 $\pm$ 4.42	18–30	head trauma
10	5 m, 5 f	31.6 $\pm$ 11.84	17–59	ICH
3	1 m, 2 f	27.0 $\pm$ 8.54	19–36	anoxic encephalopathy
3	1 m, 2 f	45.3 $\pm$ 15.69	33–63	ischemic stroke
1	male	43		brain tumor
1	male	36		drug overdose

ICH = Intracerebral hemorrhage.

infratentorially, except in 1 patient, who had infratentorial perfusion in the first test that disappeared in the second test done 24 h later. All patients eventually developed cardiac asystole despite full medical supportive care.

Fig. 2. Planar (a) and SPECT (b) images showing absence of cerebral perfusion in supratentorial and infratentorial areas consistent with the diagnosis of brain death.

Discussion

The use of radionuclide cerebral perfusion imaging studies in the confirmation of the clinical criteria for the diagnosis of brain death have been reported previously [6–9]. This study confirms the reliability of dynamic, planar and SPECT imaging for the diagnosis of brain death. We therefore hope that this study will contribute to increase awareness of clinicians in Kuwait and elsewhere, particularly those involved in intensive care and certification of suspected brain death.

Although brain death is essentially a clinical diagnosis, it is desirable to perform laboratory tests to confirm the diagnosis, particularly in cases where the clinical tests cannot be performed safely. These include patients with respiratory failure from causes such as pulmonary edema and adult respiratory distress syndrome where PaO_2 may not be raised to a level high enough to safely perform the apnea test; patients with eye injuries that may not be able to react to pupillary, corneal, or vestibulo-ocular reflex

testing accurately, and patients with perforated tympanic membranes that cannot safely undergo the ice water caloric test for assessing vestibulo-ocular reflexes.

Confirmatory tests may also be required to shorten the time interval for harvesting organs for possible transplantation. Confirmatory tests are generally neurophysiological or intracranial blood flow studies. Electrophysiological tests include electroencephalography (EEG) [10], brainstem auditory evoked responses (BAER) [11] and somatosensory evoked potentials (SSEP) [12]. The EEG primarily measures hemispheric electrical activity; BAER and SSEP assess brainstem electrical activity. The EEG alone is not an ideal confirmatory test because it may be isoelectric (flat) while the brainstem is still functioning. The BAER and SSEP are less sensitive to metabolic or toxic suppression; however, they sample only a small component of brain function in restricted sensory pathways [13]. Therefore, it is necessary for the three tests to show absence of intracranial electrical activity before brain death can be confirmed [14].

The tests that show the absence of intracranial blood flow include contrast and radionuclide angiography [13, 15], xenon-enhanced CT [16], transcranial Doppler ultrasonography [17] and radionuclide brain perfusion imaging using tracers such as ^{99m}Tc -HMPAO [18]. These tests are based on the cessation of intracranial blood flow at some time during the process of brain death. Contrast angiography is invasive, not available around the clock and exposes potential donor organs to toxic contrast media [8]. Although xenon-enhanced CT is the most reliable confirmatory test [19], it is not routinely available, due to technical problems associated with the handling of xenon-133, and in addition xenon-133 has low gamma energy (81 keV) and X-radiation (31 keV) that contributes to extracerebral flow [20].

The radionuclide brain perfusion imaging involves a simple intravenous administration of a radiotracer that diffuses across the blood-brain barrier and is extracted by the brain tissue. In the event of brain death, the cerebral tissue fails to extract the radiotracer, hence radioactivity

is not detected in the brain thereby leaving an empty box (brain death) appearance (fig. 2). Typical pathology of brain death shows a swelling from a hemispheric lesion that eventually raises the intracranial pressure above the perfusion pressure. The tentorium momentarily protects the cerebellum from the rising pressure, thereby leading to visualization of the posterior fossa when radionuclide brain perfusion is performed early as observed in 1 patient in this study and also previously reported by others [7, 8, 21].

These findings indicate that posterior fossa perfusion may be present despite definite clinical signs of brain death, probably indicating a stage in the inevitable process of death. In devastating brain injuries, the point at which a decreasing perfusion pressure seriously compromises cerebral circulation to all or a portion of the brain cannot be determined because the changes vary from area to area within the central nervous system and perhaps may explain the discrepancy between compartments [22]. However, this does not imply that in the presence of cere-

bellar perfusion, brain death based on clinical criteria should lead to withdrawal of life support or harvesting of organs before there is evidence of total lack of intracranial flow in a subsequent scan.

When dynamic phase study does not show sagittal sinus activity, performing planar and SPECT imaging is necessary to confirm the absence of activity in the parenchyma itself. Performing SPECT scan on a routine basis in patients who did not show brain radioactivity on planar images did not offer any additional advantage except when the patient has a scalp wound which could lead to false-positive perfusion in the posterior fossa, then it becomes mandatory to do SPECT scan to establish the absence of parenchymal perfusion.

Conclusion

This study showed that radionuclide brain perfusion imaging is a simple, reproducible and noninvasive test in the confirmation of brain death. Since the cost of the equipment and the need for specialized training may be prohibitive in underresourced countries, the diagnosis of brain death should rely on the well-established clinical criteria.

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