Singapore Med J 1998; Vol 39(6):247-250

Transcranial Doppler Assessment of Brain Death in Children

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ABSTRACT

Aim: To estimate the values of transcranial doppler (TCD) in the determination of brain death in children.

Method: Fifty-eight comatose children (from 2 days to 13 years, median 28 months) with Glasgow Coma Sores of ≤ 7 had TCD examinations. The waveforms and the cerebral blood flow velocities of the middle cerebral arteries (MCAs) were monitored at intervals. Electroencephalogram (EEG) was recorded continuously in 34 patients. Twenty children survived, 38 died, 17 patients met the criteria for determination of brain death by clinical and EEG criteria[15] or by clinical criteria alone[2].

The prevalence of retrograde diastolic flow (RDF) was analysed by using chi-square test.

Results: All the brain death patients displayed "special" TCD waveforms including RDF or small systolic forward flow (SFF). RDF appeared in 14, 2 and 3 patients in the brain death, non-brain death and survival group respectively. The occurrence of RDF in the brain death group was significantly higher than in the other two groups ($p < 0.01$). Persistence of RDF or SSF and direction of flow index < 0.8 in the MCAs for more than 2 hours in serious comatose children, was a reliable indicator to predict or confirm brain death. Using this criteria, no false negative or false positive results were found in this group of patients.

Conclusion: TCD has a high sensitivity and specificity in the determination of brain death in children.

Keywords: transcranial doppler (TCD) brain death, retrograde diastolic flow (RDF)

INTRODUCTION

Brain death denotes complete and irreversible cessation of brain function[1-2]. Since the advent of cardiopulmonary support for severely brain-injured patients, diagnosis of brain death has become an important issue medico-legally and socially. Determination of brain death needs not only clinical criteria, but also laboratory tests to provide objective evidence. In recent years, transcranial doppler (TCD) has shown high sensitivity and specificity in the determination of adult brain death[3-5]. It is a safe, non-invasive, bedside procedure. However, little information is available on TCD in confirming brain death in children[6-8]. The purpose of this study was to estimate the values of TCD in determining brain death in children.

PATIENTS AND METHODS

Between February 1995 and April 1996, 58 comatose children with Glasgow Coma Scores of ≤ 7 were hospitalised at the intensive care unit (ICU) of the Beijing Children's Hospital. They had TCD examinations. The test group included 35 boys and 23 girls with ages ranged from 2 days to 13 years (median 28 months). Twenty patients survived, of these 17 patients fulfilled the criteria for brain-death. The causes of coma and outcome are shown in Table I. Clinical brain death was determined according to the guidelines by the 10th National Pediatric Academic Meeting of the Chinese Medical Association held in Dandong City. These include: a) deep coma with no automotor function; b) absent pupillary and corneal response; c) no spontaneous respiration including failure to initiate respiration on apnoea trial; d) fixed heart rate, including after an atropine test; e) drugs hypothermia and endocrine or metabolic causes for coma had been excluded, and f) isoelectric electro-encephalogram (EEG) persists for more than 30 minutes. The final outcomes at the time of discharge or death were separated into three groups: brain death (n=17); non-brain death (n=21), and survival (n=20).

Bedside TCD examinations were performed by using a Medasonics Cerebral Diagnosis System with a pulsed 2 mHz Doppler probe and an integrated fast Fourier real time frequency analyser. The middle cerebral arteries (MCAs) were monitored at intervals by placing the doppler probe on to the temporal bone between the lateral margin of the orbit and the ear, about 1cm above the zygomatic arch. The measuring depth was adjusted to the previously established age dependent values[9]. Doppler evaluations were carried out at least two times a day during the period of coma and every 2 to 4 hours when they met the clinical criteria for brain death. If signals attributable to the MCA could not be found by the two independent observers, the signal was deemed to be absent. The observing index included: waveforms, systolic peak flow velocity (Vs) mean flow velocity (Vm), late diastolic peak flow velocity (Vd), pulsatility index (P1) and a direction of flow index (DFI). DFI was

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Table I – The causes of comatose and outcome of 38 patients

Causes of coma	Total No.	Outcome		
		Brain deaths	Non-brain deaths	Survival
Cerebral hypoxia	24	3	11	10
Spontaneous cerebral haemorrhage	15	8	5	2
Encephalitis	9	4	1	4
Encephalopathy	3	1	1	1
Reye's syndrome	2	0	1	1
Intracranial tumour	1	1	0	0
Near drowning	1	0	1	0
Foreign bodies in the trachea	1	0	1	0
Severe infection	2	0	0	2
Total No.	**58**	**17**	**21**	**20**

defined as: DFI=1-R/F, where R was the velocity of diastolic reverse flow, F was the velocity of the systolic forward flow.

Neurological examination, arterial pressure and body temperature were measured at the time when the Doppler readings were taken. Carbon dioxide tension was measured either from expiratory air or arterial blood samples. EEGs were recorded continuously using a Sirecust 404 electro cardio-cerebralgram monitor in 34 comatose patients with Glasgow Coma Scores of ≤ 4 (15 of the patients fulfilled the criteria of brain death). Thirty-five patients underwent one or more computed tomography (CT) scans of the brain.

The occurrence rate of RDF was analysed with chi-square test. A p value of < 0.05 was considered statistically significant. Data analysis used was done by systar statistics software. Consent was obtained from at least one parent of each patient.

RESULTS

For the brain-death group, 3 patients met the clinical criteria for brain death when the first TCD examination was performed soon after admission. The other 14 patients deteriorated to brain death gradually.

Table II – The comparison of occurrence of RDF among the brain death, non-death death and survival groups

	Brain deaths n=17	Non-brain deaths n=21	Brain deaths n=17	Survival n=20	Non-brain deaths n=21	Survival n=20
RDF	14	3	14	2	3	2
No RDF	3	18	3	18	18	18
χ^2	17.61		19.60		0.18	
	$p < 0.001$		$p < 0.001$		$p > 0.05$	

* Free degree = 1
RDF = retrograde diastolic flow

I. RDF waveform and prognosis

In the brain death group, 14 patients displayed continuous or interval RDF 4 hours to 6 days before they met the clinical criteria for brain death, with a DFI < 0.8. RDF appeared only in 2 patients in the survival group, but all of them still maintained diastolic forward flow to some degree and DFI > 0.8. In the non-brain death group, 3 patients showed RDF. Two of the 3 patients were diastolic reverse flow with forward flow, DFI > 0.8; only one patient showed diastolic reverse flow with no forward flow and DFI < 0.8 during hypotension (Table II). The results showed that the occurrence of RDF in the brain death group was significantly higher than in the other two ($p < 0.01$). No significant difference in RDF was found between non-brain death and survival groups ($p > 0.05$).

II. TCD waveforms when clinical brain death criteria was fulfilled

When the 17 deeply comatose patients met the criteria for brain death, 10 displayed RDF in the MCA bilaterally. All had diastolic reverse flow and without forward flow, DFI < 0.8; two displayed RDF over one MCA with brief small systolic forward flow (SFF) over the other MCA; 5 displayed SFF in the MCAs. In three patients, asystole occurred during period of RDF. There were 9 patients who progressed from RDF to SFF in 4 to 12 hours (median 8 hours). In 7 patients, asystole occurred during periods of SFF, the time taken for the other 7 patients from SFF progressed to no detectable single ranged from 4 to 36 hours (median 16 hours).

III. Periodic blood flow waveform and outcome

Periodic blood flow waveform is defined as TCD waveforms that fluctuate with respiration. Fourteen patients in the brain death group and 10 in the non-brain death group displayed periodic blood flow waveform 4 – 36 hours before asystole occurred. Only one case of severe asthma in the survival group showed this briefly. The patient survived and remained in a persistent decorticate state.

IV. TCD waveforms over the more severely damaged brain

In this study, TCD waveforms were significantly different between the two MCAs in the 12 comatose patients (intracerebral haemorrhage in 9, meningoencephalitis in 2, brain tumour with cardiac arrest in 1). Eight cases were confirmed to be local brain damage or diffusive brain damage. One side was noted to be more severe by CT scan. Five cases progressed to brain death. On the side where brain damage was more severe, Vm was lower, P1 was higher and RDF or SFF appeared earlier when compared to the other side.

DISCUSSION

Brain death may follow after primary brain damage or secondary brain damage after cardiopulmonary arrest. In paediatric patients, both occurred at the same time causing abnormal cerebral metabolism, cerebral oedema and intracranial hypertension. It is the main pathological basis of brain death when intracranial pressure approximates or exceeds the mean arterial pressure, causing cession of intracranial pressure reached the level of cerebral perfusion pressure and finally became zero, three types of TCD waveforms could be observed : (1) Retrograde diastolic flow; (2) very small systolic forward flow, and (3) no signal.

In our study, TCD waveforms in children with brain death clearly differed from that of normal children. All patients showed characteristically high resistance of TCD profiles. The findings revealed that during progression from brain damage to brain death, the changes of cerebral circulation from high-flow, low-resistance to high-resistance, low-flow could be clearly identified by TCD.

RDF is the most common TCD wave form in adult brain-death patients that is when ICP becomes so great that total lamina collapse occurs. There is an absence of net blood flow throughout the cardiac cycle. The "windkessel effect" permits a small degree of anterograde blood flow during systole, which is negated by retrograde blood flow during diastole. Kirkham and Mcmenamin et al[8,15] had noticed that RDF may occur when intracranial pressure elevates severely before brain death, but they lacked a systematic study. Our study reveals RDF as the most common TCD profiles in brain-death children. These often appear before they meet the clinical criteria for the determination of brain death. There is a relationship between the time of RDF appearance and the speed at which intracranial pressure increases. The slower ICP increases, the earlier RDF appears. In three patients in the brain death group who were monitored relatively late, RDF could not be observed but SFF was seen directly. The SFF waveform reflects that the cerebral circulation arrest is more serious than RDF. Although 2 cases of RDF were found in the survival group, both of them were diastolic reverse flow with forward flow in some degree, and DFI $>$ 0.8. Through positive treatment, these 2 patients' RDF disappeared in one to two hours. In the non-brain death group, 3 patients showed RDF, 2 of them were diastolic reverse flow with forward flow, DFI $>$ 0.8, another patient showed whole diastolic reverse, DFI $<$ 0.8 in the condition of hypotension soon after resuscitation. All of the three patients became asystolic before they met the clinical criteria for brain death. In our study, when a patient displayed RDF or SFF and DFI $<$ 0.8, no one recovered diastolic forward flow waveform and survived. Therefore, if in a deeply comatose child, RDF appears (especially without any diastolic forward flow) or SFF waveforms and DFI $<$ 0.8 in the period of treatment, it warns of a poor outcome and often progresses to brain death. If TCD shows diastolic reverse flow with forward flow when the vital signs are obviously abnormal such as hypotension, the possibility of survival still exists with symptomatic treatment.

Periodic waveform was not a specific indicator in determining brain death. It was a sign of severe intracranial hypertension and poor outcome. It often suggests that the patient would be asystolic within 24 hours. RDF or SFF with periodic waveform could confirm brain death more accurately.

As intracranial pressures were not completely equal in local brain damaged patients, RDF or SFF could appear earlier in one or two vessels on the severely damaged side compared to the opposite side. In some cases, arrest of intracranial blood flow may not occur at the same time in different basal cerebral arteries[3]. TCD waveforms were significantly different between the two MCAs in 12 comatose patients in this study. On the side where brain damage was more severe, RDF or SFF appeared earlier than on the other side in 7 patients, 5 of them progressed to brain death. Therefore, the diagnosis of brain death could not be based on TCD waveforms unilaterally. On the other hand, bedside TCD examination could provide some useful information about the location of brain damage for some critically ill patients when CT scanning could not be performed.

Petty et al[3] reported that the finding of either reversed diastolic flow, or small early systolic spikes in more than one intracranial artery on TCD in a comatose patient was highly specific (100%) and sensitive (91.3%) for adult brain death. Shiogai et al[4] had similar findings. It has been reported that the occurrence of false negative or positive result was relatively higher in children, especially in small infants[2, 8,16]. Jalili found that the specificity of Doppler diagnosis of brain death in children was 100% and the sensitivity was 71.4%.

In our study, all the 17 comatose children who fulfilled the clinical criteria for brain death showed RDF or SFF waveforms, DFI $<$ 0.8. No false negative was found. The sensitvity was 100%. In our experience, when the vital signs were approximately normal, persistence of RDF or SFF waveform and DFI $<$ 0.8 in the MCAs for more than 2 hours in serious comatose children monitored by TCD, was a reliable indicator for predicting or confirming brain death. Using this criteria, no false negative or false positive results were found. If a patient shows diastolic reverse flow with forward flow in the state of abnormal vital signs, the possibility of recovery still exists when the situation can be rectified quickly. It must be kept in mind that: (1) TCD is only a confirming test, clinical examination is the most important in the diagnosis of brain death; (2) when the vital signs are significantly abnormal soon after cardio-pulmonary resuscitation, the diagnosis of brain death cannot be made immediately; (3) brain death should not be diagnosed by TCD special waveforms from one cerebral vessel, and (4) TCD monitoring should be continued for more than 2 hours following the appearance of special waveforms of brain death.

CONCLUSION

This study showed that TCD has a high sensitivity and specificity in the determination of brain death in children. RDF is the most common TCD waveforms in children with brain death. TCD monitoring is a useful technique in ICU for assessing outcome and guiding treatment of comatose children. TCD can help to determine brain death earlier in order to reduce unnecessary consumption of manpower resources. Consideration for organ donation for transplantation can also be considered earlier.

ACKNOWLEDGMENTS

We would like to thank our colleagues for allowing us to conduct this study on their patients.

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