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Clinical Paper

Transcranial Doppler ultrasound in therapeutic hypothermia for children after resuscitation☆

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ABSTRACT

Aim of the study: The aim of the present study was to assess the cerebral flow in children receiving therapeutic hypothermia after resuscitation. The prognostic value of transcranial Doppler findings was correlated with the clinical outcomes in these children.
Methods: A retrospective cohort study was conducted at the paediatric intensive care unit of Chang Gung Children's Hospital between January 2011 and December 2012. All children from 1 month to 18 years of age who received therapeutic hypothermia after resuscitation were eligible. Serial transcranial Doppler examinations were performed and the findings were reviewed.
Results: Seventeen children met the eligibility criteria for this study. Fourteen patients (82.3%) were asphyxial in aetiology, and 12 (70.5%) of these cases occurred outside of the hospital. Eight patients (47.1%) had a Paediatric Cerebral Performance Score of 1 or 2 at 3 months after the events. Reversal diastolic or undetectable flow patterns during therapeutic hypothermia were associated with unfavourable prognosis. Normal mean flow velocity in the rewarming phase and normal pulsatility index in the hypothermia and rewarming phases were associated with favourable outcome.
Conclusion: The transcranial Doppler examinations provided additional information for cerebral perfusion during therapeutic hypothermia, which may in the future be used to guide changes to hypothermia management. Mean cerebral blood flow velocity and pulsatility index by transcranial Doppler sonography can serve as a prognostic factor for children who receive therapeutic hypothermia after resuscitation.

1. Introduction

The neurological prognosis after resuscitation depends on the duration and severity of global brain ischaemia and hypoxia.[1,2] An effective cerebral perfusion during cardiopulmonary resuscitation and following the return of spontaneous circulation (ROSC) has a decisive influence on the final neurological prognosis.[3,4] However, ROSC does not automatically restore normal cerebral perfusion, and therefore effective cerebral perfusion is the most important prognostic factor.[4,5] Until recently, accurate measurements of cerebral blood flow have been restricted to complex techniques such as single-photon emission computed tomography or positron emission tomography.[6] Nevertheless, these techniques are not suitable for routine use in clinical practice.

Transcranial Doppler ultrasonography (TCD), an easily applicable and bedside technique, allows for the measurement of blood flow velocities of the main cerebral arteries. Using serial TCD examinations, the cerebral haemodynamic status after resuscitation can be identified.[7] TCD examines the velocity and pulsatility of cerebral blood flow, making it possible to analyse the cerebral haemodynamic status.[6,8] The changes in mean blood flow velocities as visualised by TCD in the main cerebral arteries strongly reflects changes in the cerebral blood flow during

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cardiopulmonary resuscitation and following ROSC.[9] In addition, TCD does not interfere with therapeutic hypothermia or sedative support.[6,8]

Only a few studies have reported on TCD as a neuromonitoring option during therapeutic hypothermia in children after resuscitation. Therefore, the aim of the present study was to assess cerebral blood flow in children receiving therapeutic hypothermia after resuscitation, and to estimate the prognostic value of TCD findings for the prediction of clinical outcomes in these children.

2. Methods

2.1. Patient selection

This was a retrospective chart review of patients who had successfully been resuscitated with ROSC and received therapeutic hypothermia at the paediatric intensive care unit of Chang Gung Children's Hospital between January 1, 2011 and December 31, 2012. Cases were defined as occurring out of the hospital if chest compressions were initiated before arrival at the hospital. Cases in whom initiation of chest compressions occurred in the emergency department or other hospital setting were defined as in-hospital cardiac arrests. The patients were eligible for the study if they met the following criteria: (1) age from 1 month to 18 years; (2) duration of cardiac arrest at least 3 min and ROSC after resuscitation; (3) comatose status (Glasgow Coma Scale ≤ 8) after ROSC; and (4) survival for at least 12 h after ROSC.[10,11] We excluded the children with refractory cardiogenic shock despite the use of vasopressor and/or inotropic agents, non-coma status (GCS > 8) and known pre-existing neurological diseases which could have resulted in potential changes in baseline cerebral blood flow and/or cerebral blood flow regulation. If a patient was resuscitated more than once during the study period, only the first resuscitation meeting the eligibility criteria was included. All patients received therapeutic hypothermia within 6 h after resuscitation for a continuous period of 24 or 72 h.[10] This study was approved by the Chang Gung Memorial Hospital Institutional Review Board.

2.2. Cooling methods

Induction of therapeutic hypothermia was accomplished with thermal heat-exchange cooling pads attached to the patient and controlled by an automated temperature management system (Arctic Sun, Medivance, Inc. Louisville, CO, USA) set to the target temperature 33 °C. Rewarming was achieved by increasing the set point of the temperature management system gradually at 1 °C per day until the patient reached 36 °C.[10,11] All patients were sedated with midazolam and received neuromuscular blockers (cisatracurium to prevent shivering during treatment). Sedation and neuromuscular blockers were stopped as soon as the body temperature was $\geq$36 °C. From our past experience of critical care for neonatal asphyxia, the cooling duration was 24 h for the children with ventricular arrhythmia induced cardiac arrest, and 72 h for the children with asphyxia.[10]

2.3. Patient management and transcranial Doppler ultrasonography findings

All patients were intubated with mechanical ventilation to maintain normocarbia ($PaCO_2$ 35–40 mmHg) and to prevent cerebral vasodilatation and vasoconstriction. Age-appropriate cerebral perfusion pressure (neonates 40–50 mmHg, children 50–60 mmHg, adolescents >60 mmHg) was maintained. Because the intracranial cerebral pressure was not available, fluid boluses and vasopressors were used to achieve an alternative optimal mean arterial blood pressure (age-appropriate cerebral perfusion pressure + central venous pressure). As haemoglobin is an essential determinant of oxygen delivery, we maintained the haemoglobin level of all patients above 10 g dL^{-1}.

Table 1
The normal values and defined abnormal values for transcranial colour Doppler used in this study.

	Normal	Abnormal
MCA TAMX velocities (cm s^{-1}): mean[a]		
3–12 months	74 (±14)	>88 or <60
1–3 years	85 (±10)	>95 or <75
4–6 years	94 (±10)	>104 or <84
7–10 years	97 (±9)	>106 or <88
11–18 years	81 (±11)	>92 or <70
Pulsatility index (PI)	0.6–1.1	PI < 0.6 PI > 1.1 (including reversal diastolic flow or undetectable flow)

Table is modified from the data in Ref. 13.
MCA, middle cerebral artery; TAMX, time-averaged mean of the maximal velocities; PI < 0.6: indicating hyperaemia, vasospasm or stenosis; PI > 1.1 (including reversal diastolic flow or undetectable flow): indicating increased intracranial hypertension or cerebral asystole.
[a] The standard deviation (SD) velocities.

Serial TCD examinations of the bilateral middle cerebral arteries (MCA) were performed by a 2 MHz probe (128XP; Acuson, Mountain View, CA, USA). The examinations were performed in 3 phases: pre-hypothermia phase, hypothermia phase (12–24 h after the body temperature had reached 33 °C), and rewarming phase (12–48 h after the body temperature had reached 36 °C). The TCDs were performed by one operator (Lin JJ). For each TCD investigation, values of the peak flow systolic velocity, end diastolic flow velocity, and mean flow velocity were recorded and the pulsatility index (PI) was calculated. The normal values and defined abnormal values for mean flow velocity in the MCA used in this study were summarised in Table 1.[12,13] If the mean flow velocity was different in bilateral MCA, we chose the most severe abnormal mean flow velocity as the severity of this phase.

The PI was calculated as the ratio of the difference from systolic to diastolic velocities divided by the mean blood flow velocity. A normal PI value has been reported to range from 0.6 to 1.1.[13] We divided the PI level into three categories: low PI (PI < 0.6) indicating hyperaemia, vasospasm or stenosis; normal PI (PI = 0.6–1.1); and high PI (PI > 1.1 including reversal diastolic flow or undetectable flow) indicating increased intracranial hypertension and cerebral asystole (Table 1). If the PI was different in bilateral MCA, we chose the higher PI as the severity of this phase.

2.4. Outcome measures

The neurological outcomes were assessed by Paediatric Cerebral Performance Category (PCPC) scores in the children who survived 3 months after the events, or in those who expired at hospital. PCPC scores measure the degree of cognitive function and range from 1 to 6, where 1 is normal, 2 is mild disability, 3 is moderate disability, 4 is severe disability, 5 is coma or vegetative state, and 6 is brain death. The mortality cases were categorised as score 6. The neurological outcomes were divided into two groups according to the Paediatric Cerebral Performance Category: a good prognosis (PCPC scores of 1 or 2) and poor prognosis (PCPC scores $\geq$3).

2.5. Data management and analysis

The patient characteristics for each study group are represented as descriptive statistics, and the data are presented as mean ± standard deviation (SD). The value of the TCD findings at