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Clinical paper

Can somatosensory and visual evoked potentials predict neurological outcome during targeted temperature management in post cardiac arrest patients?

Seung Pill Choi[a], Kyu Nam Park[a,*], Jung Hee Wee[a], Jeong Ho Park[a], Chun Song Youn[a], Han Joon Kim[a], Sang Hoon Oh[a], Yoon Sang Oh[b], Soo Hyun Kim[a], Joo Suk Oh[a]

[a] Department of Emergency Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea
[b] Department of Neurology, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

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ABSTRACT

Purposes: In cardiac arrest patients treated with targeted temperature management (TTM), it is not certain if somatosensory evoked potentials (SEPs) and visual evoked potentials (VEPs) can predict neurological outcomes during TTM. The aim of this study was to investigate the prognostic value of SEPs and VEPs during TTM and after rewarming.

Methods: This retrospective cohort study included comatose patients resuscitated from cardiac arrest and treated with TTM between March 2007 and July 2015. SEPs and VEPs were recorded during TTM and after rewarming in these patients. Neurological outcome was assessed at discharge by the Cerebral Performance Category (CPC) Scale.

Results: In total, 115 patients were included. A total of 175 SEPs and 150 VEPs were performed. Five SEPs during treated with TTM and nine SEPs after rewarming were excluded from outcome prediction by SEPs due to an indeterminable N20 response because of technical error. Using 80 SEPs and 85 VEPs during treated with TTM, absent SEPs yielded a sensitivity of 58% and a specificity of 100% for poor outcome (CPC 3–5), and absent VEPs predicted poor neurological outcome with a sensitivity of 44% and a specificity of 96%. The AUC of combination of SEPs and VEPs was superior to either test alone (0.788 for absent SEPs and 0.713 for absent VEPs compared with 0.838 for the combination). After rewarming, absent SEPs and absent VEPs predicted poor neurological outcome with a specificity of 100%. When SEPs and VEPs were combined, VEPs slightly increased the prognostic accuracy of SEPs alone. Although one patient with absent VEP during treated with TTM had a good neurological outcome, none of the patients with good neurological outcome had an absent VEP after rewarming.

Conclusion: Absent SEPs could predict poor neurological outcome during TTM as well as after rewarming. Absent VEPs may predict poor neurological outcome in both periods and VEPs may provide additional prognostic value in outcome prediction.

Introduction

Despite advances in cardiopulmonary resuscitation (CPR) and critical care medicine, early prediction of neurological outcome for patients resuscitated from cardiac arrest is still challenging. Before targeted temperature management (TTM) is incorporated as a standard therapy for cardiac arrest patients, bilateral absence of the N20 component in the median nerve somatosensory evoked potentials (SEPs) recorded on days 1–3 or later after CPR has been reported to accurately predict poor outcome [1]. However, the predictive value of SEPs recorded within 24 h of initiating TTM has not been fully revealed. Visual evoked potentials (VEPs) are reliable prognostic indicators for perinatal asphyxia [2]. Normal and abnormal/absent VEPs are associated with normal and abnormal outcome, respectively [3,4]. Yet VEPs have not been used as an outcome predictor for adult cardiac arrest patients, and it is not known whether VEPs are influenced by TTM. Therefore, we investigated the prognostic value of SEPs and VEPs during TTM and after rewarming and whether

* Corresponding author at: Department of Emergency Medicine Seoul St. Mary's Hospital, 222, Banpo-daero, Seocho-Gu, Seoul, 137-701, Republic of Korea.
E-mail address: emsky@catholic.ac.kr (J.S. Oh).

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VEPs can provide additional prognostic value to SEPs for patients treated with TTM.

Methods

Patients

This study was reviewed and approved by the local ethics committee of our hospital. Between March 2007 and July 2015, we retrospectively studied adult patients (≥18 years) admitted to the emergency department of Yeouido St. Mary's Hospital (a university teaching hospital in Seoul, Korea) who were treated with TTM after successful resuscitation from out-of- or in-hospital cardiac arrest. All unconscious patients who were resuscitated from non-traumatic cardiac arrest were eligible for the TTM irrespective of initial rhythm. The exclusion criteria for the TTM were trauma, intracranial haemorrhage, haemodynamic instability unresponsive to volume resuscitation and vasopressor treatment, known terminal illness, poor pre-arrest neurologic status and a "do not attempt resuscitation" order. Cooling was initiated to achieve a target temperature of 33 °C using cold saline and an endovascular cooling device (CoolGard Thermal Regulation System, Alsius Corporation, Irvine, CA, USA) or external cooling device using self-adhesive gel-coated pads (Arctic Sun, Bard Medical, Louisville, CO, USA). Sedation (midazolam, 0.08 mg/kg intravenously) and paralysis (rocuronium, 0.8 mg/kg intravenously) were administered for shivering control, followed by continuous infusion of midazolam (0.04–0.2 mg/kg/h) and rocuronium (0.3–0.6 mg/kg/h). After a 24 h period of maintenance, patients were slowly rewarmed to normothermia at a rate of 0.25 °C/h. Sedation and paralysis were stopped at 35 °C. SEPs and VEPs were recorded during TTM and after rewarming in these patients following the clinical pathways and the protocol of our hospital. The patients were evaluated in terms of age, gender, cause of death, if the collapse was witnessed, if a bystander performed CPR, the initial electrocardiogram (ECG), the initial Glasgow Coma Scale (GCS) score, the initial neurologic examination, the body temperature when an EP was performed, the time between evoked potentials and ROSC, and the cerebral performance category (CPC) score at discharge (Table 1). Good neurologic outcome was defined as CPC 1-2 (no or moderate disability) and poor neurologic outcome as CPC 3-5 (severely disabled, comatose, or dead).

SEP recordings

SEPs were recorded using a Viking IV (Nicolet Instruments, Madison, WI, USA) during TTM and after rewarming of the patients. EEG disk electrodes were placed at both Erb's points, spinous process C7 and C3′ and C4′ following the International 10–20 system with skin electrode impedance below 5 kΩ. They were referenced to the mid frontal region at Fz. All patients were examined bilaterally. Electrical stimulation (impulse duration 0.2 ms; stimulation rate 3–5 Hz; and intensity 7–15 mA) was delivered overlying the median nerve at the level of the wrist. At least 200 stimulations were averaged per recording. In each SEP, the latencies to N9, N13 and N20 and the cervicocortical conduction time and N20-P23 amplitude were evaluated. SEPs were classified as SEP absent (bilaterally absent cortical N20 responses after left and right median nerve stimulation in the presence of a cervical potential), SEP present (cortical N20 response present on at least one side), or indeterminable (technically insufficient recording).

VEP recordings

VEPs were recorded from a single active electrode at Oz referenced to Fz. The stimulus was a binocular flash from light-emitting diode (LED) goggles that were placed over the patient's closed eyes. Impedances were kept below 5 kΩ. A band pass of 0.5–100 Hz was employed. Stimulation frequency was 1.3 Hz and two averages of 100 stimulations were repeated to yield reproducible results for each patient. In each VEP, the latencies to N75, P100 and N145 and N75-P100 amplitude were evaluated. VEPs were classified as VEP absent (bilaterally absent cortical P100 responses) or VEP present (cortical P100 response present on at least one side).

Statistical analysis

Quantitative data was given as the mean and standard deviation or the median and interquartile range and qualitative data as counts and percentages. Chi-square test was used to assess qualitative data. *T*-test or Wilcoxon signed rank sum test was used to compare the quantitative data. To evaluate the prognostic value of SEPs and VEPs, receiver operating characteristic (ROC) analysis was performed. Means of left and right evoked potentials were used for calculations of latencies and amplitudes. Amplitudes and laten-

Table 1
Patients demographics and clinical characteristics.

	Total patients (n = 115)	Good neurological outcome (n = 31)	Poor neurological outcome (n = 84)	p
Male	77 (67.0%)	23 (74.2%)	54 (64.3%)	0.316
Age	54.7 ± 16.6	50.2 ± 16.3	56.4 ± 16.5	0.077
Witnessed arrest	70 (60.9%)	25 (80.6%)	45 (53.6%)	0.008
Bystander CPR	41 (35.7%)	15 (48.4%)	26 (31.0%)	0.083
Shockable rhythm	17 (14.8%)	11 (35.5%)	6 (7.1%)	<0.001
Cardiac cause	48 (39%)	25 (80.6%)	23 (27.3%)	<0.001
OHCA	109 (94.8%)	29 (93.5%)	80 (95.2%)	0.718
GCS after ROSC	3 (3, 3)	3 (3, 5)	3 (3, 3)	<0.001
Absent PLR after ROSC	63 (54.7%)	8 (25.8%)	55 (65.5%)	<0.001
Absent CR after ROSC	104 (90.4%)	23 (74.2%)	81 (96.4%)	0.001
Time from ROSC to EP during TTM (n = 85) (h)	21.0 ± 6.7	19.9 ± 7.3	21.5 ± 6.4	0.299
Time from ROSC to EP after rewarming (n = 90) (h)	70.2 ± 20.5	74.3 ± 23.1	68.3 ± 19.2	0.204
Body temperature when EP during TTM (n = 85) (°C)	33.0 ± 0.6	33.3 ± 0.5	32.9 ± 0.7	0.027
Body temperature when EP after rewarming (n = 90) (°C)	36.8 ± 0.7	36.9 ± 0.5	36.7 ± 0.8	0.247
Neurological outcome at discharge CPC 1	27 (23.5%)	27 (87.1%)	0 (0.0%)	
CPC 2	4 (3.5%)	4 (12.9%)	0 (0.0%)	
CPC 3	1 (0.9%)	0 (0.0%)	1 (1.2%)	
CPC 4	35 (30.4%)	0 (0.0%)	35 (41.7%)	
CPC 5	48 (41.7%)	0 (0.0%)	48 (57.1%)	

Values are presented as mean ± SD, median (IQR), and frequency (%). CPR: cardiopulmonary resuscitation, OHCA: out-of-hospital cardiac arrest, GCS: Glasgow Coma Scale, PLR: pupillary light reflex, CR: corneal response, ROSC: return of spontaneous circulation, EP: evoked potential, TTM: targeted temperature management.