The Effect of Lumbar CSF drainage on the Neurologic Outcome Improvement in OHCA underwent TTM

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1. Introduction

Global cerebral ischaemic-reperfusion brain injury following cardiac arrest (CA) can lead to intracranial hypertension and, occasionally, acute brain swelling [1,2]. Even small increases in brain volume due to oedema can result in harmful increases in intracranial pressure due to the brain's rigid encasement. The previous studies demonstrated a higher intracranial pressure (ICP) was strongly associated with and seemed predictive of a poor outcome, and higher ICP following global cerebral ischaemia immediately after ROSC, and severe blood-brain barrier (BBB) disruption began at 24 h after ROSC in the poor neurologic outcome group treated with target temperature management (TTM) [3, 4].

Several therapeutic approaches have been established for the treatment of increased ICP in traumatic brain injury, including TTM, elevation of the head, sedation, volume resuscitation, maintenance of adequate arterial oxygenation, cerebrospinal fluid drainage via a ventriculostomy, moderate hyperventilation, and mannitol administration [5]. However, despite these various therapies, a considerable number of patients remain nonresponsive to aggressive management strategies. During the last decades, controlled lumbar cerebrospinal fluid (CSF) drainage has been considered to be contraindicated in the setting of increased ICP because of the possibility of transtentorial or tonsillar herniation [6–8]. In contrast, a recent report on the use of lumbar CSF drainage to treat refractory increased ICP suggested that this controversial therapeutic strategy might be efficient and a valuable treatment when applied to carefully selected patients had discernible basal cisterns and controlled release of CSF under monitoring of ICP and vital signs [9, 10]. Plus, much of the CSF volume is present in the subarachnoid spaces and cisterns around the brain. This CSF is not accessible for drainage by ventriculostomies but is accessible by lumbar drainage [11].

However, to the best of our knowledge, there is no study on the effect of lumbar CSF drainage to improve neurologic outcome in CA patients treated with TTM. We aimed to evaluate the effect of lumbar CSF drainage on neurologic outcome in post-CA patients treated with TTM.

2. Methods

This study was approved by the Institutional Review Board of the Chungnam National University Medical Centre (CNUH IRB 2019-07-033-003). We obtained approval and consent from the next of kin before enrolment.

2.1. Study design and patients

This was a prospective single-centre study conducted from November 2019 to October 2021 on patients who had been treated with TTM following CA. The primary endpoint was to evaluate the effect of the lumbar CSF drainage on attenuation of brain swelling and improvement of the neurologic outcome in post-CA patients treated with TTM. The data were collected from the electrical medical record. We named the patients were treated with our standard protocol as the non-lumbar CSF drainage group, whereas the patients treated with the protocol and the lumbar CSF drainage were called as the lumbar CSF drainage group. The neurologic status of the patients was obtained on the 6-month follow-up after return of spontaneous circulation (ROSC). Neurological outcome was assessed using the Glasgow-Pittsburgh cerebral performance categories (CPC) scale. The good outcome group was defined as a CPC 1 or 2, and the poor outcome group as a CPC between 3 and 5. Resuscitated cardiac arrest patients whose Glasgow coma scale (GCS) was 8 or less after the return of spontaneous circulation (ROSC), and who underwent TTM were included in the study. The exclusion criteria for this study were as follows: (1) < 18 y of age, (2) traumatic CA or interrupted TTM (due to haemodynamic instability), (3) not eligible for TTM (i.e., intracranial haemorrhage, active bleeding, known terminal illness, or poor pre-arrest neurological status), (4) ineligible for LP (i.e., brain computed tomography showed severe cerebral oedema, obliteration of the basal cisterns, occult intracranial mass lesion, or coagulopathy: platelet count < 40 x 10^3/mL or international normalized ratio (INR) > 1.5),[12] (5) on extracorporeal membrane oxygenation, (6) unable to consent to LP, and (7) refusal of further treatment by the next of kin.

2.2. TTM protocol

We have applied our protocol and TTM using cooling devices (Arctic Sun ® Energy Transfer Pads TM, Medivance Corp., Louisville, USA) for patients who had sustained ROSC since March, 2016. Our protocol was as follows; (1)the target temperature of 33°C was maintained for 24 h with rewarming to 37.0°C at the rate of 0.25°C/h, (2) was monitored using an oesophageal and bladder temperature probe, (3) sedatives and analgesics were used during TTM and patients received standard care according to the protocol described in a previous study included deep sedation, (4) mild hyperventilation (PaCO2 35~45 mmHg), (5) mean arterial pressure (MAP) was maintained between 80 and 110 mmHg via vasoactive support with norepinephrine and, if needed, plasma volume expansion with crystalloids, (6) adequate arterial oxygenation between 150 and 250 mmHg, (7) patients were placed in supine position with 30° head-up tilt, (8) anti-epileptic medications were administered as soon as a seizure was suspected either clinically or through EEG [13].

2.3. Data collection

The following data were collected from the database: age, sex, presence of a witness at the time of the collapse, bystander cardiopulmonary resuscitation (CPR), first monitored rhythm, aetiology of cardiac arrest, time from collapse to CPR (no flow time), time from CPR to ROSC (low flow time), sequential organ failure assessment (SOF) score, ICP measured on immediate after ROSC, time from ROSC to inserting a lumbar drainage catheter placed through the lumbar vertebral interspace into the subarachnoid space (ICP time), , and CPC at 6 months after ROSC.

2.4. ICP control via lumbar CSF drainage

We have performed the lumbar CSF drainage on the level of the lumbar spine between L3 and L4 with the patient lying in the lateral decubitus position with hips and knees flexed. A lumbar drainage catheter was inserted using a Hermetic™ lumbar accessory kit (Integra Neurosciences, Plainsboro, NJ, USA) in the patients. ICP monitoring via lumbar drainage catheter was practiced using the *LiquoGuard*® (Möller Medical GmbH & Co KG, Fulda, Germany). ICP control strategies was initiated when ICP exceeded 15 mmHg in the absence of noxious stimuli at the rate of 10~20 ml/h via a lumbar drainage catheter

until ICP was less than 15 mmHg [14, 15].

2.5. MRI protocol and analysis

Our hospital has a standardised magnetic resonance imaging (MRI) protocol for non-traumatic OHCAs. MRI imaging includes diffusion weighted image (DWI), and apparent diffusion coefficient (ADC) map. The MRI was obtained between 72–96 h after ROSC. Forty contiguous DWI sections per patient were acquired using a 3T scanner (Achieva 3 T; Philips Medical System, The Netherlands). The standard of b=1000 s/mm^2 was used for all DWIs. ADC maps were created from the mono-exponential calculation of DWI with a commercial software and workstation system (Leonardo MR Workplace; Siemens Medical Solutions, Erlangen, Germany). For quantitative analysis of ADC to evaluate the effect of lumbar CSF drainage on attenuation of brain swelling, images were processed and analysed using software (FMRIB Software Library, Release 5.0 (c) 2012, The University of Oxford) that can extract brain tissue by eliminating cranium, optic structure, and extra-cranial soft tissues. Images were retrieved in Digital Imaging and Communications in Medicine format from picture archiving and communication system servers at the hospital and were converted to NITFI format using MRIcron (http://www.nitrc.org/projects/mricron). ADC thresholds ranged from 0 to 1590 X 10^{-6} mm^2/s to exclude artefacts or pure CSF [16]. The percentage of voxels (PV) meant number of voxels below different ADC thresholds was divided by total number of voxel.

The % voxels of ADC values (PV)

$$PV = \frac{Voxel\ numbers\ of\ ADC\ value\ {}_{0}^{ADC\ threshold}}{Voxel\ numbers\ of\ ADC\ value\ {}_{0}^{1590}}$$

2.6. Sample size

A previous study reported ICP on 24 h after ROSC was 13.22 ± 3.99 mmHg in good outcome and 18.57 ± 5.61 mmHg in poor outcome [17], 62 patients were needed to achieve the power of 0.99 at a significance level of 0.05 (two-sided test).

2.7. Statistical analysis

We reported continuous variables as median with interquartile range or as mean and standard deviation depending on the normal distribution. Categorical variables were reported as frequencies and percentages. We performed the propensity score matching with age, sex, presence of a witness at the time of the collapse, bystander CPR, first monitored rhythm, causes of CA, no flow time, low flow time, sequential organ failure assessment (SOFA) score, and ICP on immediate after ROSC between both groups. Comparisons between the two groups were made using the chi-square test, Fisher's exact test, the Mann-Whitney U test, or two-tailed *t*-test. Multivariate logistic regression models were built to identify the effect of the lumbar CSF drainage on the neurologic outcome. Kaplan-Meier analysis was performed to evaluate the effect of the lumbar CSF drainage on the neurologic outcome at 6 months after ROSC. The estimated odds ratio was considered to assess risk. All statistical analyses were performed using the PASW/SPSSTM software, version 18 (IBM Inc., Chicago, USA). Results were considered significant at $P < 0.05$.

Conflict of interest statement: The authors have no conflict of interest to report

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