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Regional cerebral blood flow and cellular environment in subarachnoid hemorrhage: A thermal doppler flowmetry and microdialysis study

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ABSTRACT

Background: Cerebral microdialysis enables assessment of regional metabolic physiology and provides biomarkers for clinical correlation in critical conditions, such as subarachnoid hemorrhage (SAH). The aim of our current study was to investigate the correlation between regional cerebral blood flow and microdialysis parameters (glucose, lactate, glycerol, pyruvate concentrations, and lactate/pyruvate metabolic ratio) in patients with SAH.

Materials and methods: Twenty-one patients with SAH were enrolled in our retrospective study. Cerebral blood flow (CBF) based on thermal diffusion methodology, the thermal coefficient *K*, and microdialysis biochemical markers were recorded. The duration of the brain monitoring was 10 days.

Results: Microdialysis glucose concentration was inversely related to the cerebral temperature and to the L/P ratio. Furthermore, it was positively correlated to all other microdialysis parameters but glycerol. The *K* coefficient was strongly and positively correlated with the temperature and marginally with the CBF. The L/P ratio was positively correlated with glycerol, while it was inversely correlated with the CBF. Patients who died had elevated L/P ratio and *K* coefficient compared to the survivors in our series.

Conclusions: Thermal conductivity coefficient may change over time as cerebral injury progresses and tissue properties alter. These alterations were found to be associated with the microdialysis metabolite concentrations and the CBF itself. The microdialysis biochemical indices of cell stress and death (glycerol, L/P ratio) were positively related to each other, while the measured L/P metabolic ratio was higher among patients who died.

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1. Introduction

Subarachnoid hemorrhage (SAH) accounts for 3% of all strokes, and 5% of all stroke deaths [1]. It is estimated that over 25% of potential life years lost secondary to stroke, may be attributed to SAH [2]. Despite the great advances in the diagnosis of SAH, mortality remains high (around 50%), while approximately one third of survivors have an unfavorable neurological and functional outcome [3]. Monitoring of cellular environment's events has unveiled critical biochemical processes, and has helped in predicting cerebral vasospasm, thus allowing early intervention [4–6]. It is estimated that approximately 70% of the patients with aneurysmal SAH develop angiographic vasospasm, while extracellular alterations in glutamate, lactate, lactate/pyruvate ratio, and glycerol concentrations have been associated with delayed cerebral ischemia following aSAH [4–6]. Microdialysis monitoring enables assessment of regional cerebral metabolic physiology, and provides biomarkers for clinical correlation [7,8]. Most available data in the pertinent literature come from traumatic brain injury (TBI) patients, however its utilization in the setting of aSAH has also been demonstrated [9].

The purpose of our present study was to investigate the correlation between cerebral blood flow and microdialysis parameters [glucose, lactate, glycerol, pyruvate values and lactate/pyruvate ratio (L/P)] in patients with SAH.

2. Materials and methods

All patients with CT proven diagnosis of recent onset SAH, with or without intraventricular hemorrhage (IVH), admitting Glasgow Coma Scale (GCS) score ≤ 8, and undergoing invasive multi-parametric microdialysis monitoring were considered for enrollment in our retrospective clinical study, with prospectively set criteria. The protocol of our current study was approved by the Institutional Review Board. All the patients' data were handled according to the Helsinki and the HIPAA acts. A detailed written consent form was obtained by each patient's next of kin, for participating in our study.

Our inclusion criteria were: CT proven SAH diagnosis of recent onset (less than 24 h since symptoms started), GCS score upon admission ≤8, age >18 years. Patients with age >80 years, brain dead patients, patients with impending brain death, patients with abnormal clotting studies upon admission, patients with chronic renal failure, and patients with known malignancy history were excluded from our study. Our study covered a 5-year period (from 2009 to 2013).

Complete demographic data, family and detailed past medical history of every patient were recorded at admission, followed by a thorough neurological examination.

A total of 21 patients met our inclusion criteria, out of the 37 patients admitted during the same period with the diagnosis of SAH in our institution. All patients were sedated, intubated and mechanically ventilated. A minimally invasive, multiparametric, neuromonitoring system was introduced within the first 8 h after admission to the ICU department. A frontal burr hole was placed at Kocher's point under sterile conditions, and a three way-bolt kit (Licox bolt kit, Integra NeuroSciences, Plainsboro, NJ, USA) was inserted. This bolt kit was used for insertion of: (a) an intracranial pressure (ICP) measurement catheter (Codman microsensor kit, Codman, Johnson & Johnson, MA, USA), (b) a brain tissue-oxygen monitoring catheter ($PbrO_2$ measuring catheter, Licox, Integra NeuroSciences, Plainsboro, NJ, USA), and (c) a microdialysis catheter (CMA 70 Brain Microdialysis Catheter, 10 mm membrane length, 20 kDa cut off, CMA, Stockholm, Sweden). The catheters were placed in the intact brain parenchyma, and ipsilateral to the most prominent pathology area. The proper catheter position was confirmed with a brain CT scan, which was obtained within 24 h following the catheter's implantation.

A second burr hole was placed approximately 1–1.5 cm anteriorly to the previously described one, and was used for inserting a Cerebral Blood Flow (CBF) catheter (QFlow 500 Perfusion Probe, Hemedex, Cambridge, MA, USA). This catheter is flexible, biocompatible, and radio-opaque, of ~1 mm (3 French/19 gauge) diameter, which is inserted into the brain parenchyma for measuring regional cerebral blood flow. This catheter is FDA approved for cerebral monitoring for up to 10-days. The distal tip of the catheter was tunneled subcutaneously and was secured with sutures, 3–4 cm distal to the entry point, as to minimize the risk of infections. The data obtained are displayed on a bedside monitoring device (Bowman Perfusion Monitor, Hemedex, Cambridge, MA, USA) on a real time basis. This monitoring system provides CBF calculations by employing a thermal diffusion methodology, as this is expressed by the following equation: $CBF = K(1/V - 1/V0)$, where CBF is expressed in ml/100 g/min, V is the voltage gradient between the two electrodes, $V0$ is the voltage gradient under zero flow, and K constitutes a constant representing the brain parenchyma thermal conductivity [10]. Additionally Brain Water Content (BWC) data can be extrapolated from the measurements. In our study BWC data were provided by the Hemedex Company (Hemedex, Cambridge, MA, USA).

The duration of this multi-parametric brain monitoring was 10 days in all of our patients. After this period the catheters were removed. In those patients that there was indication for further ICP monitoring, this was performed by inserting a new intraparenchymal ICP fiberoptic catheter. All the obtained data, including ICP, brain temperature, concentrations of lactate, pyruvate, glucose, glycerol, and the L/P ratio, as well as the CBF measurements, and the K coefficient were recorded and analyzed. Moreover, the Simplified Acute Physiology Score II (SAPS II), and the Predicted Death Rate (PDR) scores were calculated and recorded.

All patients were treated using a cerebral perfusion pressure (CPP) guided protocol. The patients' outcome was evaluated with the Glasgow Outcome Scale (GOS) score at discharge, and then at 3 and 6 months post-discharge, via either a detailed neurological examination in our outpatient clinic, or via a telephone interview performed by one of the residents of our neurosurgery department.

2.1. *Statistical analysis*

The statistical analysis was performed using the program SPSS 22.0v. (Statistical Package for Social Sciences, IBM, Chicago, IL,

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