CASE STUDY

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Chronic Cerebral Perfusion Pressure Monitoring in Freely Moving Rats

Introduction

Cerebral perfusion pressure (CPP) plays a vital role in maintaining oxygenation of cerebral tissues. CPP is a calculated measurement derived from subtracting Mean Arterial Pressure (MAP) from Intracranial Pressure (ICP), with normal levels ranging from 60 – 80 mmHg. Altered regulation of CPP levels, < 50 mmHg, can result in cerebral ischemia and irreversible damage.[1] Decreased levels are typically caused by increases in cerebral edema due to trauma or space-occupying lesions, or a hypotensive crisis like sepsis or shock. Management and stabilization of CPP during crisis are critical in preventing irreversible brain damage, which can lead to permanent disability or death.

The Challenge

In both preclinical and clinical settings, accurate CPP can only be monitored invasively for a short period of time in unconscious patients or anesthetized animals. In research models, anesthetized and acute monitoring is incapable of providing a realistic picture of the relationship between ICP and MAP under physiological conditions. In addition, current methods to chronically monitor increased ICP, particularly in rodents, have been challenging.[2] To overcome the challenges, researchers conducted a pilot study using implantable telemetry to monitor both ICP and MAP simultaneously in awake and freely moving rats for chronic monitoring of CPP.

The Study

Sixteen male Wistar strain rats were divided into two groups of eight: a control group and an experimental group. The experimental group received water intoxication through fractionated hyperhydration combined with the administration of desmopressin, an antidiuretic, inducing cerebral edema. Subjects were prepared with dual pressure telemetry transmitters (HD-S21, Data Sciences International). For ICP, one pressure sensor was placed into the intracranial space through the right frontal bone and 2mm in front of the bregma. The second pressure sensor was inserted into the right carotid artery, close to the base of the cranium. This location was chosen to obtain MAP as close as possible to the ICP measurement, reducing possible errors caused by animal positioning. Telemetry data was acquired continuously for 72 hours and analyzed (Ponemah 6.2, Data Sciences International).

The Results

In the water intoxicated rats, telemetry recordings averaged considerably higher ICP, MAP and CPP compared to the control group (fig. 1). The experimental group displayed a homeostatic response to cerebral edema with increases in MAP, resulting in maintained average CPP levels above 70 mmHg throughout the study (fig. 2).

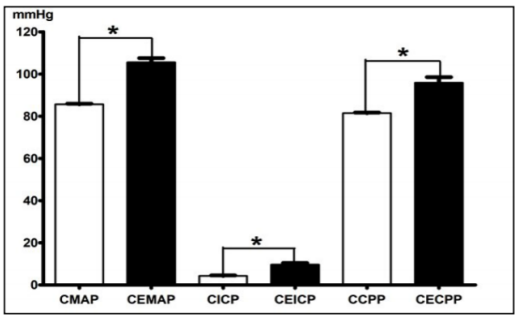

Figure 1: ICP, MAP and CPP average values over 72 hours mean ± SEM, significant differences are given, * $p < 0.5$

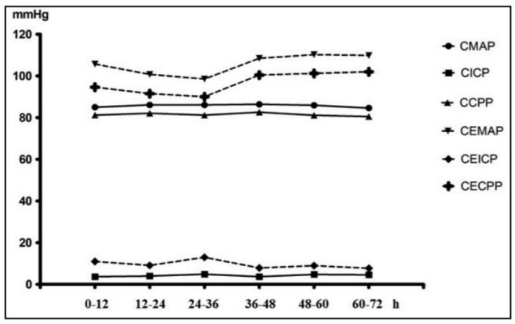

Figure 2: ICP, MAP and CPP fluctuations over 72 hours
Solid lines = control group; Dotted lines = experimental group

Amplitude differences in the ICP and MAP curves between control and experimental groups were observed, with the experimental group displaying a lower amplitude (fig. 3,4). This difference is supported by previous studies on induced cellular brain edema.

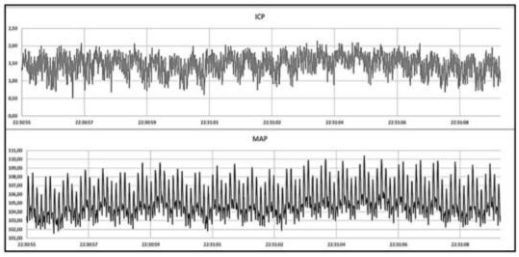

Figure 3: 13 second snapshot of ICP and MAP in control group

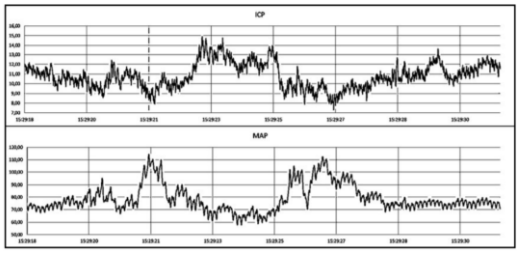

Figure 4: 12 second snapshot of ICP and MAP
in experimental group

The Successes

This study was conducted to validate continuous telemetry for chronic monitoring of CPP in an experimental model. Telemetry is commonly cited in publications for monitoring both ICP and MAP in rodents separately. Researchers utilized dual pressure telemetry technology to monitor both pressures simultaneously in the same animal, allowing them to calculate chronic CPP. Continuous ICP and MAP data gave a first ever look into CPP levels over a 72-hour period in unrestrained and conscious rats. Monitoring CPP over longer periods allow researchers to gain new insight on the relationship between ICP and MAP, resulting in advanced treatments and improved patient outcomes. In addition, unrestrained and conscious methods enhance animal welfare, while providing a more translational research model.

DSI

Data Sciences International (DSI) offers complete systems that sense, transmit, acquire, and report physiologic data. To create a more robust study design, scientists rely on DSI technology to study specific targets as well as obtain a holistic view; allowing them to look at side effects upstream or downstream of the main pathology.

The DSI team ensures researchers are equipped and prepared from the first minute of their study to the last, because your research is everything.

References:

[1] Prabhakar H, Sandhu K, Bhagat H, Durga P, Chawla R. Current concepts of optimal cerebral perfusion pressure in traumatic brain injury. J Anaesthesiol Clin Pharmacol. 2014;30(3):318-327. doi:10.4103/0970-9185.137260

[2] Eftekhari S, Westgate CSJ, Uldall MS, Jensen RH. Preclinical update on regulation of intracranial pressure in relation to idiopathic intracranial hypertension. *Fluids Barriers CNS*. 2019;16(1):35. Published 2019 Nov 26. doi:10.1186/s12987-019-0155-4

Kozler P, Maresova D, Pokorny J. Intracranial pressure and mean arterial pressure monitoring in freely moving rats via telemetry; pilot study. Neuro Endocrinol Lett. 2019 Dec;40(7-8):319-324. PMID: 32304368.