Autoregulatory capacity and compensatory reserve in an experimental model of acute shunt failure

Kiran J. Agarwal-Harding¹, Marek Czosnyka, Ph.D.²

¹Harvard Medical School, Oliver Wendell Holmes Society, Class of 2013, ²Neuroscience Unit, Department of Clinical Neurosciences, Addenbrooke Hospital, University of Cambridge

Abstract

Hydrocephalus arises due to increased intracranial pressure (ICP), which may result in death. Autoregulation and the compensatory reserve in cases of most brain injuries are important for the maintenance of cerebral perfusion pressure (CPP), which is critical for brain function. In this study, we investigated the autoregulatory capacity and compensatory reserve in an experimental model of acute shunt failure.

Introduction

Hydrocephalus and acute shunt failure

- Affects pediatric and adult patients
- It is the most common reason for neurosurgery in children in the United States
- Incidence is even higher in developing countries
- Preferred treatment is placement of a ventriculoperitoneal shunt
- 50% of VP shunts fail within 2 years
- Failure of the VP shunt can lead to life-threatening acute intracranial hypertension (IICH)

Cerebral autoregulation

- Occurs to maintain steady cerebral blood flow (CBF) and cerebral perfusion
- Perfusion is inversely related to intracranial pressure (ICP)
- Autoregulation can be overwhelmed, leading to tissue damage and poor prognosis
- High ICP plateau-waves are clinically related to poor patient outcomes
- Investigation has been done into noninvasive means of measuring autoregulation to monitor patients with ICH

Calculated physiological parameters: LDx, PRx, PAX, RAP

- Parameters that have been shown to indicate autoregulatory capacity of small vessels and the compensatory reserve in the cerebral vasculature
- Calculated using data that can be obtained noninvasively
- Have been shown individually to correlate in a clinical setting with ICP changes
- Further work is necessary to determine the research seen in these parameters with controlled increased intracranial pressure that is extravascular in origin

Objectives

- Determine the ability of various physiological calculated parameters to report increases in ICP and indicate brain health
- Determine the validity of various physiological calculated parameters to approximate health ranges of CPP

Hypothesis

- Deep intracranial hypertension will cause an increase in LDx, PRx, PAX, and RAP as autoregulation is compromised by high ICP and the compensatory reserve of small blood vessels is depleted.
- The parameters LDx, PRx, PAX, and RAP will indicate ranges of healthy CPP in the rabbit where autoregulation is occurring appropriately.

Significance

- Application to patients with acute shunt failure and acute hydrocephalus
- Understanding the physiology of disease can help determine the risks these patients face and potential treatments
- Validation of these parameters as tools in assessing autoregulation in small vessels
- Application to patients with any form of intracranial hypertension including stroke, traumatic brain injury, and cerebral malaria

Current ICP monitoring is invasive, discontinuous, and requires skilled professionals
- Noninvasive monitoring would be cheaper, safer, and more widely applicable in the clinical setting

Methods

Experimental Model

- New Zealand White Rabbits
- Basilar artery dependent cerebral perfusion (bilateral common carotid ligation)
- Mock CSF (saline 0.9%) infused into subarachnoid space at site of lumbar puncture
- Infusion was continued at a controlled rate to elevate ICP until a Cushing response was seen

Monitoring of...
- ICP: intraparenchymally inserted transducer
- ABP: transducer in radial artery
- Arterial blood inflow velocity: TCD insonation of MCA (FVx)
- Laser Doppler Flowmetry (LDF)
- PaCO2: from ventilator

Sample of raw recording data

Data processing

- Antifacts removed manually
- Regions of baseline ICP and regions where the Cushing response was evident were identified manually and removed
- Parameters (LDx, PRx, PAX, RAP) were calculated using raw data
- All parameters had a calculation period of 5 minutes with an update period of 10 seconds

Calculations

- LDx
  o Correlation coefficient between CPP and LDF
  o Indicates autoregulatory capacity in small vessels as measured at the cortex using laser Doppler flowmetry
- PRx
  o Correlation coefficient between ICP and CPP
  o Indicates compensatory reserve
- PAX
  o Correlation coefficient between CPP and the amplitude of the ICP waveform
  o Indicates compensatory reserve
- RAP
  o Correlation coefficient between ICP and the amplitude of the ICP waveform
  o Indicates compensatory reserve

Binned analysis

- 55 rabbits
- Values analyzed for full range of ICP and CPP
- Figures show values averaged across ranges of ICP and CPP
- Means are calculated for patients that required less than 2% of the data
- For all parameters showing a linear regression, the correlation coefficient was calculated, the coefficient was transformed using the Fisher transform, and the significance was tested (p<0.05)

Comparative analysis

- Paired analysis of 51 rabbits
- All parameters when ICP<25mmHg compared to when ICP>25mmHg
- Figures show mean values for the specified variable, error bars show some standard deviation
- Paired t-tests were performed on the means to test for a significant difference for each variable before and during Cushing response (p<0.05)

Results

Binned Analysis

Summary

- ABP increases with increasing ICP, as expected
- ABP decreases with decreasing CPP indicating poorly controlled blood pressure in the experimental model, possibly due to the trauma of the experimental preparation
- HR decreases with increasing ICP, as expected, and HR v. CPP mirrors this same trend
- Amplitude of the ICP waveform decreases with increasing ICP, as expected, and Amp. ICP v. CPP mirrors this same trend
- FV v. CPP demonstrated Lassen curve showing optimal CPP range
- LDx, PRx, PAX, and RAP all increase significantly with increasing ICP indicating a loss of autoregulation in small vessels and compensatory reserve as ICP increases
- RAP in particular shows a trend of increasing to a maximum as compensatory reserve is depleted
- LDx, PRx, PAX all show a parabolic relationship with CPP, indicating an optimal range of CPP where these parameters are minimized (between 50 and 90mmHg)
- RAP shows a loss of compensatory reserve as ICP increases and as CPP decreases

Comparative Analysis

Discussion

- During CSF volume expansion ICH, cerebral autoregulation occurs in the small vessels to maintain CPP
- LDx, PRx, PAX, and RAP are useful parameters in determining optimal ranges of CPP in patients with acute shunt failure
- These parameters change with changing ICP and can be monitored continuously and noninvasively
- These parameters may prove helpful in managing patients with hydrocephalus and other ICH-related illnesses

Acknowledgements

Special thanks to Dr. Peter Smielewski, Dr. Magdalena Kasprzick, and Dr. Enrico Sorrentino at the University of Cambridge for help with data collection and analysis. Thank you also to the National Institutes of Health Graduate Partnership Program and Harvard Medical School Office of Enrollment Programs.

References