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Assessment of Cerebrovascular Resistance with Model of Cerebrovascular Pressure Transmission

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SUMMARY

A two step modeling method of cerebrovascular pressure transmission, the dynamic relationship between arterial blood pressure (ABP) and intracranial pressure (ICP) has been developed as a means to continuously assess cerebrovascular regulation and resistance. Initially, system identification modeling was used to construct a numerical model of cerebrovascular pressure transmission. Next, the modal frequencies of the numerical model and the actual ABP recording were used to manipulate the parameters of a physiologically-based biomechanical model such that: 1) the actual and simulated ICP; and 2) the numerical and biomechanical model modal frequencies match. This study was designed to compare changes of cerebrovascular resistance of the biomechanical model with the expected changes of cerebrovascular resistance associated with the occurrence of either a plateau wave or refractory intracranial hypertension.

Pressure recordings from five patients with plateau waves and five patients with intracranial hypertension were used. Vascular resistance decreased significantly during the plateau wave and was inversely related to CPP, indicating active vasoreactivity. In contrast, vascular resistance increased significantly during intractable intracranial hypertension and was directly related to CPP, indicating impaired cerebrovascular regulation. Such results support the use of the modeling method as a means to continuously assess changes of cerebrovascular regulation and resistance.

INTRODUCTION

Clinical methods designed to provide continuous assessment of regulation of cerebral blood flow (CBF) and further insight into evolving pathophysiological processes during the intensive care management of patients with brain injury are needed. The approach of this study to address these needs is based on serial modeling of cerebrovascular pressure transmission as defined by the dynamic relationship between arterial blood pressure (ABP) and intracranial pressure

(ICP). Biomechanical models of intracranial pressure dynamics based on the Monroe-Kellie doctrine (which assumes the total volume within the craniospinal sac remains constant) have been developed to simulate ICP dynamics and hemodynamic alterations (1,9,10). In contrast to these biomechanical models which require physiological compatibility, the use of numerical system identification modeling has been proposed recently as a method to continuously assess regulation of cerebral blood flow (4). This procedure is a strictly numerical one in which the digitized paired input/output values are coupled to a generalized dynamic description of a process to produce a simulated output that matches the actual output by minimization of the least squares difference between the actual and simulated digitized output series (6). The two step modeling method of cerebrovascular pressure transmission has been developed to continuously assess cerebrovascular regulation and resistance. Initially, system identification modeling is used to construct a numerical black-box model of cerebrovascular pressure transmission. Next, the modal frequencies of the numerical model and the actual ABP recording are used to manipulate the parameters of a physiologically-based biomechanical model such that: 1) the actual and simulated ICP; and 2) the numerical and biomechanical model modal frequencies are matched.

In this study two distinct clinical conditions associated with traumatic brain-injured patients, the plateau wave and intractable intracranial hypertension were studied. The plateau wave is a pathophysiological event that is characterized by a sudden rapid elevation of ICP followed by a sustained period of elevation that is terminated by a rapid decrease in ICP (2,7,8). The onset of the wave has been described by a vasodilatory cascade phase which links active vasodilation, increased cerebral blood volume, elevated ICP and decreased cerebral perfusion pressure (CPP) (8). The relatively rapid termination of the wave has been described by a vasoconstriction cascade phase in which active vasoconstrictive events lead to decreases in cerebral blood volume and ICP and an increase of CPP (8). Intractable intracranial hypertension is a pathophysiological condition that is characterized by an uncontrollable increase of ICP and a decrease in CPP which leads to compression of the vascular bed and ischemic levels of cerebral blood flow (CBF). The aim of this study was to use the two-step modeling method on pressure recordings obtained during plateau waves and during intractable intracranial hypertension as a means to derive values of simulated arterial/arteriolar bed resistance (SimR) and determine whether changes in this resistance were consistent with those expected to occur for each pathophysiological condition.

METHOD AND MATERIALS

Pressure recordings sampled at a rate of 30 or 50 Hz from two groups of five patients each were used in this study. One group demonstrated plateau waves; while the other group demonstrated a prolonged increase of ICP characteristic of intractable intracranial hypertension. Neurocritical Care Users Committee, Addenbrooke's Hospital, Cambridge, United Kingdom approved the fact that physiological signals were recorded numerically and since this did not introduce any additional risk or burden to routine patients care, individual consent was not required at the time of recording. Each set of recordings was labeled in such a manner that the patients could not be identified by the Memphis group. The Institutional Review Board at The University of Memphis approved the data analysis protocol.

The first step of the two step modeling procedure, system identification modeling, has been previously reported in detail (4,5). Briefly a modified biomechanical model proposed by Czosynka and his colleagues (1) was used to provide a generalized dynamic differential equation of cerebrovascular pressure transmission. A system identification technique was applied to each 500 paired samples of digitized pressure recordings to obtain the modal frequencies of cerebrovascular pressure transmission. For the brief period on which each numerical model is based, perturbations of ABP and ICP are assumed to be small and

cerebrovascular pressure transmission is considered to be linear and time-invariant. In the second step, mean values of the modal frequencies derived by the first step numerical model for each three consecutive 500 sample modeling intervals of ABP recording are applied to the physiologically-based biomechanical model to simulate an ICP recording for the recording interval based on 1500 samples. Using the physiologically-based biomechanical model, a computational method was constructed to simulate ICP for the ABP recording and the corresponding numerically derived modal frequencies for each modeling interval. The computation was designed to manipulate the resistance and compliance elements of the biomechanical model such that the minimum square error for the 1500 sample interval between: 1) the actual and simulated ICP recordings; 2) the numerical model value of the highest modal frequency (HMF) and the biomechanical value of HMF; and 3) the numerical model value of a dampening factor (DF) of the lower modal frequencies and the DF of the biomechanical model were minimized. Compliance and resistance elements were allowed to range over values consistent with those reported in previously published modeling studies of intracranial pressure dynamics (9,10,1). The parameters of the biomechanical model were estimated by recursive computation to obtain a best fit set which produced a minimum least square error and maximum correlation value for each segment of the pressure recording.

RESULTS

ICP recordings obtained from a patient during the demonstration of a plateau wave and of a patient with intractable intracranial hypertension are shown (see Fig. 1). Throughout the three phases of the plateau wave ABP did not change significantly while ICP increased and CPP decreased relative to baseline during the wave; at the termination of the wave, ICP decreased and CPP increased (see Table 1). Throughout intracranial hypertension ABP did not change while ICP increased and CPP decreased (see Table 1).

For the ICP recordings of a plateau wave and intractable intracranial hypertension, changes in the values of HMF of both models and the corresponding changes in simulated arterial-arteriolar bed resistance are shown in Figure 2. The derived HMF values of the numerical system identification model and the corresponding HMF values of the biomechanical model increased at the onset of the plateau wave during vasodilation and decreased at termination during the constrictive phase of the wave (see Fig 2a). Consistent with the active changes in the cerebrovasculature during the wave, the corresponding simulated values of arterial-arteriolar bed resistance decreased at the onset of the wave and increased at the termination of the wave (see Fig. 2b). Correlations between simulated bed resistance and CPP overall, prior to, during, and after the plateau wave were 0.97 (± 0.01), 0.97(± 0.01), 0.98 (± 0.02), and 0.97 (± 0.02) respectively with a level of significance for each individual correlation at $p < 0.001$. The HMF values derived by the first step numerical model and the corresponding HMF values of the biomechanical model decreased during intractable intracranial hypertension (see Fig. 2c). Consistent with vasoconstriction at the periphery of the arterial tree during intractable intracranial hypertension, simulated resistance of the arterial-arteriolar bed progressively increased (see Fig. 2d). Mean correlations ($\pm$ S.D.) between simulated bed resistance and CPP overall, at the start, and end of the intractable intracranial hypertension recording were -0.98 (± 0.02), -0.98 (± 0.04) and -0.98 (± 0.04) respectively with a level of significance for each individual correlation of $p < 0.001$.

Overall mean values and corresponding standard deviations of ABP, ICP, CPP, HMF, and simulated resistance of the arterial-arteriolar bed and correlation of HMF with simulated cerebrovascular resistance of both groups of patients demonstrated results similar to those described by the above individual examples. For the five patients with plateau waves, mean ABP did not change during the recording period. However during the plateau wave, ICP increased and CPP decreased. Also during the plateau wave, HMF increased while simulated

vascular resistance decreased. Prior to, during, and after the plateau wave, simulated resistance of the arterial-arteriolar bed was strongly correlated to CPP, which is indicative of active cerebrovascular regulation. In contrast, for the group of patients with intractable intracranial hypertension, mean ICP at the end of the recording period was higher than at the start of recording; while mean CPP decreased over the period. Furthermore, mean HMF decreased while simulated bed resistance increased. Finally, the correlations between simulated vascular resistance and CPP at the start and the end of the recording were strongly inverse, indicating impaired cerebrovascular regulation of cerebral blood flow.

DISCUSSION

The major finding of study is that a novel two step modeling method based on ICP and ABP recordings available in the intensive care setting can be used to continuously assess changes in cerebrovascular resistance. For the five patients in the plateau wave group, simulated arterial-arteriolar vascular resistance decreased during the vasodilatory phase of the wave and increased during the vasoconstrictive phase of the wave. Two findings based on the recordings obtained from these patients indicate that regulation of CBF was intact during the recording period. First, simulated vascular resistance was directly correlated with CPP. And second, HMF was inversely related to CPP which is also consistent with intact cerebrovascular regulation as reported in laboratory study of percussive brain injury (4). In contrast the group of five patients with intractable intracranial hypertension had findings indicative of impaired cerebrovascular regulation. For all patients in this group, simulated arterial-arteriolar bed resistance steadily increased as CPP decreased. The correlation between simulated arterial-arteriolar bed resistance and CPP was strongly inverse and the HMF was directly correlated with CPP. While the change in the resistance of arterial-arteriolar bed is different for these distinct pathophysiological events, the correlation between HMF and simulated arterial-arteriolar bed resistance was strongly inverse for all patients.

Previous black-box numerical modeling of cerebrovascular pressure transmission based on clinical pressure recordings obtained during the occurrence of a plateau wave or during intractable intracranial hypertension have demonstrated that values of HMF are inversely related to CPP when cerebrovascular regulation is thought to be intact and directly related when cerebrovascular regulation is likely lost (3). In this study of clinical recordings of ABP and ICP obtained during the two distinct pathophysiological conditions, the described two-step modeling method of cerebrovascular pressure transmission was used to obtain simulated values of arterial-arteriolar bed resistance. Indicative of active vasoreactivity, in addition to demonstrating the inverse relationship between HMF and CPP, simulated bed resistance was shown to increase with CPP during the plateau wave. In contrast, during intractable intracranial hypertension a direct relationship between HMF and CPP existed and simulated bed resistance was shown to decrease with increasing CPP, indicative of impaired cerebrovascular regulation.

Possible limitations of the proposed methodology with respect to the development of a clinical application should be considered. First, the modal frequencies of cerebrovascular pressure transmission are not solely dependent on arterial-arteriolar bed resistance, but on all the resistance and compliance elements of the model. However, except for extremely high values of ICP, because arteriolar resistance is nearly ten times the magnitude of venous resistance, the simulated bed resistance has a dominant influence on the modal frequencies of cerebrovascular pressure transmission. A second limitation is that the method requires artifact free continuous dynamic recordings of ICP and ABP. Alteration of the dynamic pulsatile pressure recordings either by the inherent design of the recording instrumentation or by sensor alteration during monitoring will corrupt the modeling process. In such cases an otherwise highly pulsatile ICP recording with sharp peaks might be recorded as a rounded pulse and the computations based on cerebrovascular pressure transmission would be erroneous.

In conclusion, independent of whether the two step process modeling method of cerebrovascular pressure transmission was based on pressure recordings obtained either during a plateau wave or during intractable hypertension, the relationship between HMF and simulated resistance of the arterial-arteriolar bed was an inverse one. Pressure recordings obtained during the plateau wave demonstrated: 1) a positive correlation between CPP and simulated arterial-arteriolar vascular resistance; and 2) an inverse relationship between HMF and CPP, indicative of intact cerebrovascular regulation (4). In contrast, pressure recordings obtained during intracranial hypertension demonstrated: 1) a negative correlation between simulated vascular resistance and CPP; and 2) a direct relationship between HMF and CPP, indicative of impaired cerebrovascular regulation (4). The results of this study provide a preliminary basis for the use of the proposed modeling method of cerebrovascular pressure transmission as a means to continuously assess cerebrovascular regulation and interpret changes of cerebrovascular resistance of the arterial-arteriolar bed.

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Figure 1. ICP Recordings of Plateau Wave and Intractable Intracranial Hypertension and Brief Interval of Actual and Simulated ICP

a) ICP Recording during Plateau Wave. Arrow indicates the location of wave used for extracting 16.7 s interval of ICP recording shown below. b) Extracted ICP Recording at Arrow Located in Recording of Plateau Wave. c) Simulated ICP Recording of Biomechanical Model. d) ICP Recording during Intractable Intracranial Hypertension. Arrow indicates location used to extract 10.0 s interval of ICP recording. e) Extracted ICP Recording at Arrow Located on Recording of Intractable Intracranial Hypertension. f) Simulated ICP Recording by Two Step Modeling Method of 10 s Extracted ICP Recording.

Figure 2. Changes of HMF Values of Numerical and Biomechanical Models and Simulated Arterial-Arteriolar Bed Resistance During Plateau Wave and Intractable Intracranial Hypertension

a) Derived HMF Values for ICP Recording with Plateau Wave. For each three consecutive values of HMF, the mean value and standard deviation was computed and are plotted as closed squares with corresponding error bars. The corresponding HMF values of the biomechanical model are plotted as closed circles. Correlation between model HMF values was strong and significant at 0.98, and $p < 0.001$. b) Simulated Values of Arterial-Arteriolar Bed Resistance for ICP Recording with Plateau Wave. HMF values and simulated arterial-arteriolar bed resistance were inversely related with a slope of the regression line relationship of 1.38 mmHg/ml/s. c) Derived HMF Values for ICP Recording of Intractable Intracranial Hypertension. Mean and standard deviation of three consecutive values of HMF of numerical model (closed squares) with corresponding error bars and corresponding HMF values of the biomechanical model (closed circles) with error bars are plotted. Correlation between model HMF values was strong and significant at 0.97 and $p < 0.0001$. d) Simulated Values of Arterial-Arteriolar Bed Resistance for ICP Recording with Intractable Intracranial Hypertension. HMF values and simulated arterial-arteriolar bed resistance were inversely related with a slope of the regression line relationship of -2.08 mmHg/ml/s.

Table 1
Overall Mean Values (+/-S.D.) Values of ABP, ICP, CPP, HMF, Simulated Resistance of the Arterial-Arteriolar Bed and Correlation of HMF Value with Bed Resistance

Condition	N	ABP (+/-SD)	ICP (+/-SD)	CPP (+/-SD)	HMF (+/-SD)	Sim. Resist. (+/-SD)	SimR vs CPP r-value (+/-SD)
-	-	mmHg	mmHg	mmHg	Hz	mmHg/ml/s	-
Plateau Wave	-	-	-	-	-	-	-
Prior	5	100.7 (+/-13.9)	27.1 (+/-2.4)	73.6 (+/-2.5)	7.5 (+/-1.1)	8.6 (+/-1.1)	0.97 (+/-0.01) ³
During	5	108.5 (+/-9.6)	44.4 (+/-4.4) ¹	67.1 (+/-3.1) ²	15.3 (+/-3.0) ¹	4.1 (+/-1.3) ¹	0.98 (+/-0.02) ³
After	5	100.4 (+/-7.1)	25.7 (+/-3.1) ¹	76.1 (+/-3.2) ¹	6.9 (+/-2.1) ¹	9.8 (+/-1.3) ¹	0.97 (+/-0.02) ³
Intractable ICP	-	-	-	-	-	-	-
Start	5	129.2 (+/-6.3)	65.6 (+/-3.8)	64.1 (+/-3.1)	16.4 (+/-0.3)	5.1 (+/-0.62)	-0.98 (+/-0.01) ³
End	5	135.3 (+/-5.2)	98.1 (+/-2.5) ¹	43.9 (+/-3.8) ¹	5.4 (+/-0.8)	12.4 (+/-1.4) ¹	-0.98 (+/-0.04) ³

¹Level of significance between mean values at p<0.001
²Level of significance between mean values at p<0.005
³Level of significance of each individual correlation (n=5) at p<0.001