Effect of subarachnoid hemorrhage on intracranial pulse waves in cats

ERICO R. CARDOSO, M.D., F.R.C.S.(C), KESAVA REDDY, M.D., AND DEEPAK BOSE, M.D., PH.D.

Departments of Surgery, Pharmacology and Therapeutics, and Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

The influence of vasoconstrictors of intracranial arteries on the amplitude and configuration of the intracranial pulse wave (ICPW) was investigated. Continuous pressure recordings from the descending aorta (systemic arterial pressure) and the third cerebral ventricle (intracranial pressure) were obtained from anesthetized cats. Computerized analysis of the configuration, amplitude, and frequency spectrum of ventricular wave (ICPW) and aortic pulse wave (SAPW) was performed. Artificial cerebrospinal fluid (CSF), blood, or 5-hydroxytryptamine (5-HT) was injected intracisternally. In 24 control cats, 2 ml artificial CSF was injected into the cisterna magna. This produced a significant increase in amplitude of the ICPW but no change in the SAPW. Ten animals received 14 intracisternal injections of 2 ml autologous blood which caused narrowing of the amplitude of the ICPW as well as of all its components (P1, P2, and P3), with no significant change in the SAPW's. Eight animals were also subjected to cisternal injection of 2 ml of a 10^-4-M solution of 5-HT, resulting in findings similar to those produced by autologous blood. Frequency spectrum of the intracranial and aortic pulse waves showed a high degree of correlation between wave amplitudes and height of the fundamental wave in the FFT record.

These results suggest that the cerebral vasospasm that follows cisternal injections of blood and 5-HT in cats can be diagnosed by analysis of the ICPW. This method may allow early diagnosis and continuous monitoring of cerebral vasospasm in humans.

KEY WORDS: subarachnoid hemorrhage · intracranial pressure · intracranial pulse wave · intracranial vasospasm · cat

The carotid and vertebral arterial pulsations enter the cranium and travel through large conducting arteries, small intraparenchymal arteries, and arterioles. Simultaneous retrograde pulsations are transmitted from the jugular veins to the intracranial bridging and cortical veins. Pulses generated from each of these structures are also transmitted to the cerebrospinal fluid (CSF) to form a composite intracranial pulse wave (ICPW). Thus, the configuration of the wave obtained through an intraventricular catheter results from the temporal summation of various simultaneous wave components generated from all of the pulsatile intracranial vessels.

Under physiological conditions, the incoming arterial pulses are the main contributors to the configuration of the ICPW. Thus, narrowing of the caliber of large conducting intracranial arteries, as observed after subarachnoid hemorrhage (SAH) or subarachnoid injection of 5-hydroxytryptamine (5-HT), should alter the amplitude and configuration of the ICPW. We investigated this hypothesis.

Materials and Methods

Animal Preparation

Twenty-nine adult mongrel cats were included in this study. Anesthesia was induced by intraperitoneal injection of 30 mg/kg body weight of sodium pentobarbital (Nembutal) and maintained with a continuous intravenous infusion of approximately 25 mg/hr. The infusion rate required individual adjustments in order to maintain a stable level of anesthesia. The right femoral artery and vein were cannulated. The arterial catheter was introduced as far as the descending aorta and connected to a pressure transducer* for continuous monitoring of systemic arterial pressure.

* P50 pressure transducer manufactured by Statham Instruments, Hato Rey, Puerto Rico.
Effect of SAH on intracranial pulse waves in cats

monitoring. A tracheostomy was then performed. The animal was next paralyzed by intravenous injection of gallamine (Flaxedil, 10 mg/kg body weight/hr) and artificially ventilated by means of a Harvard animal respirator.† Arterial blood gas levels were checked throughout the experiment and kept within normal limits. Rectal temperature was monitored by a rectal probe;‡ the animal's temperature was maintained at approximately 38°C by the use of a thermal blanket interposed between the animal and the operating table.

The animal was then turned to the prone position and its head secured in a stereotaxic head-holder. A No. 16 metal needle was placed 1 mm lateral to the midline and 10 mm anterior to the intermeatal line through a drill hole in the skull. This blind-ended needle had a distal side-hole aimed posteriorly and positioned stereotaxically into the third ventricle, located 15 mm from the outer skull table when the needle was at an angle of 1.5° with the vertical.¶ A hard polyethylene catheter 15 cm in length with an inner diameter of 2 mm was interposed between the needle and a miniature pressure transducer,§ which was kept at the level of the third cerebral ventricle. A similar catheter was used for systemic arterial pressure (SAP) monitoring. The entire fluid-filled system was thoroughly checked for the presence of air bubbles. The lines were intermittently flushed to avoid artefactual narrowing of wave amplitudes. The intracranial pressure (ICP) line was flushed with 0.05 ml of artificial CSF and the SAP line with 0.5 ml of heparinized saline.

**Subarachnoid Injections**

The cisterna magna was cannulated percutaneously with a No. 20 catheter,¶ held by self-retaining holders and used for manual subarachnoid injections of test solutions. Control animals received 2 ml of artificial CSF at physiological pH and temperature, injected manually into the cisterna magna. Cerebral vasospasm was induced by cisternal injections of 2 ml of fresh autologous arterial blood or 2 ml of a 10⁻⁴-M solution of 5-HT* in artificial CSF at physiological pH and temperature. In order to avoid artefactual magnification of the ICPW secondary to diminished intracranial compliance, the following measures were taken: 1) recordings were made 30 minutes after injections, when the mean ICP had returned to normal values; 2) second injections were given 60 minutes after the first one; and 3) the same volumes of artificial CSF, 5-HT solutions, or blood were given to the control and experimental groups.

**Data Processing**

Pressure and pulse-wave data were stored on an instrumentation tape recorder for later analysis on a waveform analyzer coupled with an Apple II computer.† The values for pulse-wave amplitude and wave components were averaged from three consecutive ventricular waves (ICPW's) and aortic pulse waves (SAPW's) recorded during respiratory expiration. The three main components of the ICPW, namely P₁, P₂ and P₃, were identified, and their amplitudes were measured separately.¶ Values obtained during baseline and experimental conditions were compared.

**Spectral Analysis of ICPW and SAPW**

Spectral analysis of ICPW's and SAPW's was done from stored analog data, which were then digitized at a rate of 2 kHz for a total of 4096 points. The digitized data were analyzed by a fast Fourier transform algorithm in the digital waveform analyzer. Very low frequency components, related to cyclic respiratory waves, were excluded from the analysis. The spectral components consisted of a fundamental wave (F) and three other higher-order harmonic components. The amplitude of the spectral components was correlated with the amplitude of the ICPW's and SAPW's as measured in the time domain.

**Statistical Analysis**

Data have been expressed as the mean and standard error of the mean. A two-tailed paired t-test was applied to compare significant differences of wave amplitudes before and after each event.

**Results**

**Pulse-Wave Configuration**

Subarachnoid injection of artificial CSF did not alter the configurations of the ICPW or the SAPW. On the other hand, subarachnoid injections of blood and 5-HT produced narrowing of the ICPW amplitude without altering the configuration of the SAPW (Fig. 1).

**Wave Measurements**

There were wide individual variations of baseline values of ICPW amplitude. Thus, comparison of average results prior to and after each maneuver does not reflect the extent of change for each animal. In order to eliminate misleading results by comparing animals with very different baseline ICPW's, the changes of ICPW are taken as a percentage change from the base-

† Harvard animal respirator manufactured by Harvard Apparatus, Millis, Massachusetts.
‡ Tele-thermometer manufactured by Yellow Springs Instrument Co., Yellow Springs, Ohio.
§ Miniature P50 gold pressure transducer manufactured by Gould Inc., Oxnard, California.
¶ Cathlon IV catheter manufactured by Criticon Canada Inc., Markham, Ontario, Canada.
* Serotonin supplied by Sigma Chemical Co., St. Louis, Missouri.

† Teac XR-30 video recorder, Model 3-7-3, obtained from Naka-Chô, Musashino, Tokyo, Japan; Data 6000 waveform analyzer manufactured by Data Precision, Boston, Massachusetts.
Simultaneous recordings of blood pressure (BP) and intracranial pressure (ICP) waves during baseline conditions (upper), after subarachnoid injection of artificial cerebrospinal fluid (center), and following subarachnoid hemorrhage (SAH, lower). There are minimal changes of the BP wave configuration, while the ICP wave undergoes major amplitude narrowing following SAH.

Subarachnoid injections of artificial CSF in 34 experiments changed the mean ICPW amplitude from $0.46 \pm 0.05$ to $0.49 \pm 0.04$ mm Hg. This represented a $20.47\% \pm 8.75\%$ increase in amplitude when each change was compared to its baseline value. The mean ICP changed minimally, from $3.46 \pm 0.6$ to $3.13 \pm 0.52$ mm Hg. The SAPW amplitude changed from $36.48 \pm 2.15$ to $37.34 \pm 2.51$ mm Hg. This represented a $3.6\% \pm 3.88\%$ increase from baseline. Thus, artificial CSF injections increased the ICPW amplitude, but produced no significant alteration of mean ICP or SAPW amplitude.

Subarachnoid injection of blood (SAH) in 14 experiments reduced the mean amplitude of the ICPW from $0.84 \pm 0.1$ to $0.63 \pm 0.1$ mm Hg. This represented a significant mean individual decrease of $25.21\% \pm 7.94\%$ ($p < 0.002$) in amplitude, when each value was taken as a percentage change from each individual baseline value. The amplitude of SAPW underwent no significant alteration: while the mean value changed from $30.43 \pm 4.74$ to $29.96 \pm 4.42$ mm Hg, the individual mean percentage change in relation to baseline values decreased by $5.11\% \pm 10.49\%$. The mean ICP changed from $2.8 \pm 0.9$ to $2.65 \pm 1.02$ mm Hg. The reduction of the ICPW produced by SAH and 5-HT was significantly different from the changes caused by artificial CSF ($p < 0.003$ and $p < 0.03$, respectively).

Subarachnoid injection of a $10^{-4}$M solution of 5-HT in eight experiments reduced the ICPW amplitude in a manner similar to that observed following SAH. The mean amplitude of the ICPW decreased from $0.41 \pm 0.06$ to $0.32 \pm 0.05$ mm Hg, while the amplitude of the SAPW increased from $38.97 \pm 5.86$ to $40.84 \pm 6.41$ mm Hg. When the difference in amplitude was calculated as an individual percentage change from baseline values for each separate event, there was a $21.37\% \pm 7.9\%$ decrease of the ICPW amplitude, while the SAPW amplitude increased by $5.2\% \pm 8.45\%$. The mean ICP decreased from $2.8 \pm 0.9$ to $2.65 \pm 1.02$ mm Hg. The drop in ICPW amplitude was significantly different from the changes caused by artificial CSF ($p < 0.003$ and $p < 0.03$, respectively).

Spectral Analysis of ICPW Waveform

Reduction of ICPW amplitude measured in the time domain correlated well with the amplitude decrease of the fundamental wave on the FFT data ($r = 0.92$) but not with the other harmonic waves. Similarly, changes in SAPW amplitude correlated well with alterations in amplitude of the fundamental wave in all three groups of animals ($r = 0.86$ to 0.89). There was no correlation with the other harmonics.

Discussion

Methods of ICPW Analysis

The ICPW has been extensively analyzed in the time domain, by which method the wave amplitude is displayed in the ordinate as a function of time on the abscissa. Thus, the temporal se-
Effect of SAH on intracranial pulse waves in cats

The injected volume of 2 ml was chosen to allow the diffuse spread of blood or 5-HT over the entire cerebral hemispheres, thus resembling a severe clinical SAH.

**Arterial Pulsation Beyond Area of Spasm**

Cerebral arterial pulse pressure beyond a spastic segment has not been measured directly but is expected to be reduced as there is reduction in the mean pulse pressures distal to the site of severe arterial stenosis of the carotid artery.\(^{15,60}\) This change is proportional to the length of the stenosed segment.\(^{37}\) Furthermore, data from cerebral blood flow studies following post-SAH cerebral vasospasm in cats show decreased blood supply to arteries beyond the spastic segment, resulting from reduction in post-stenotic arterial pressure.\(^{4,29,29,45,55}\)

Direct pressure measurements from cerebral arteries were not performed in the present experiments in order to avoid artefacts created by skull opening and subarachnoid spilling of blood.

**Intracranial Compliance and ICPW Amplitude**

The configuration of the ICPW depends upon the state of intracranial compliance as well as the incoming arterial pulsations and the retrograde venous pulses.\(^{2,5,6,10,12,25,31,33,39,47,52}\) Large volumes injected into the subarachnoid space of cats may lead to decreased intracranial compliance and consequent artefactual increase in the ICPW amplitude.\(^{5,12}\) In this study, the measures taken to avoid artefactual misinterpretations of this kind resulted in minimal alterations of the mean ICP, which were comparable for artificial CSF, blood, or 5-HT. Thus, changes of the intracranial compliance could not explain the alteration observed in the amplitude of the ICPW.

While the mean ICP was similar in all animal groups, the baseline ICPW amplitude prior to SAH was higher than that in the other groups. This was probably related to injections of artificial CSF given prior to the final injection of blood.

**Origin of Intracranial Pressure**

The configuration of the ICPW results from the temporal summation of distinct pulse-wave components originated from each of the pulsatile intracranial vascular structures.\(^{5,8,10,11,14,25,34,46}\) The extracranial arterial pulses travel through the carotid and vertebral arteries, then enter the intracranial space and are transmitted from large conducting arteries to smaller intraparenchymal arteries and arterioles. Pulsations from each of these intracranial vessels are also transmitted into the surrounding CSF, where they are usually recorded for clinical purposes. A venous pulsation is also added to each arterially generated pulse.\(^{6,25,26,54}\) This venous contribution originates from retrograde transmission of systemic venous pulsations through jugular veins and intracranial sinuses. Thus, the resulting ICPW has components originating from large conducting intracranial arteries, small intraparenchymal vessels, and...
Although the multiple origin of the ICPW has been well defined, the temporal distribution of its components as well as the relative contribution of each component are still a matter of controversy. Most investigators agree that, within homeostatic limits, the arterial input is the most significant feature. However, when there is loss of autoregulation or severe venous hypertension, the venous component becomes the main contributor to the final configuration of the ICPW.

The results of this study suggest that the narrowing of the ICPW amplitude produced by SAH or 5-HT was likely due to reduced amplitude of cerebral arterial pulsations secondary to post-SAH vasospasm. These findings reinforce the argument that the configuration of the ICPW depends mainly on incoming arterial pulsations.

**ICPW Analysis in Diagnosis of Clinical Vasospasm**

Analysis of the ICPW has been used for continuous monitoring of intracranial hydrodynamic alterations that occur with changes in the cerebral microcirculation, intracranial compliance, and elevated ICP. These changes affect mainly the midportion of the ICPW, leaving the P. component relatively unaffected. Cerebral vasospasm, on the other hand, seems to decrease the amplitude of all components of ICPW. Continuous monitoring of the ICPW with serial measurements of the ICPW amplitude of its spectral components may allow diagnosis and monitoring of human cerebral vasospasm.

Doppler ultrasonography has been developed into a reliable noninvasive method to detect and monitor human cerebral vasospasm. Furthermore, these methods allow single measurements but not continuous monitoring. The invasiveness of cerebral angiography limits its application for diagnosis and precludes its use for monitoring of the intensity of human vasospasm. The use of angiography is justifiable only when vasospasm has already been suspected from the existence of clinical symptoms or signs of secondary ischemia. Transcranial Doppler ultrasonography has been developed into a reliable method to detect and monitor human cerebral vasospasm. However, early results seem to show a lack of correlation between severity of spasm and increase in blood flow velocity (RW Seiler, unpublished data).

Ventriculostomy is frequently indicated for CSF drainage as well as for continuous ICP monitoring following severe SAH. Use of the method described here allows continuous monitoring of alterations of cerebral veins as well as for continuous ICP monitoring following severe SAH. The use of the method described in this study suggests that the narrowing of the ICPW amplitude produced by SAH or 5-HT was likely due to reduced amplitude of cerebral arterial pulsations secondary to post-SAH vasospasm. These findings reinforce the argument that the configuration of the ICPW depends mainly on incoming arterial pulsations.

**References**

17. Di Rocco C: Hydrocephalus and cerebrospinal fluid configuration and amplitude of the ICPW that may result from cerebral vasospasm. It remains to be shown whether human cerebral vasospasm will lead to changes of the ICPW similar to the ones observed in cats, because human vasospasm is usually localized as compared to the more diffuse vasospasm observed in cats.

**Acknowledgments**

The authors are indebted to Mrs. Elizabeth Reddy and Mr. Darryl Hayes for technical assistance.
Effect of SAH on intracranial pulse waves in cats


J. Neurosurg. / Volume 69 / November, 1988

Manuscript received July 24, 1987. Accepted in final form March 25, 1988. This work was supported by the St. Boniface Hospital Research Foundation and by private donations from Mr. John Wiebe and the family of Mr. Roy Hodges.

Address reprint requests to: Erico R. Cardoso, M.D., F.R.C.S.(C), Section of Neurosurgery, Health Sciences Centre, GC404, 700 William Avenue, Winnipeg, Manitoba R3E OZ3, Canada.