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Pulse Amplitude and Volume-pressure Relationships in Experimental Hydrocephalus

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Summary

The bolus injection test was used to study the intracranial volume-pressure relationships in an experimental population of normal and hydrocephalic dogs. Hydrocephalus was developed by means of an intracisternal injection of a kaolin powder solution. Hydrocephalic animals were tested a mean of 15 days after kaolin injection. The intraventricular pressure (ICPo) and amplitude of intraventricular pulse wave (AMPo) were measured at baseline steady-state. Pressure-volume index (PVI) and intracranial compliance (C) were calculated from bolus injection tests. The ICPo ($p < 0.01$) and AMPo ($p < 0.001$) were much higher in hydrocephalic animals and C decreased significantly ($p < 0.001$). There were no statistical differences regarding PVI. A direct linear correlation was found between AMPo and ICPo ($p < 0.001$) and between PVI and ICPo ($p < 0.05$) but no correlations were found between PVI and AMPo. The regression analysis showed a non-linear correlation between C and ICPo ($p < 0.01$) and between C and AMPo ($p < 0.001$). The results of our experimental study suggest that: 1) pulse amplitude relates to the intracranial compliance, and 2) the intracranial compliance is a better parameter of the volume-pressure response than PVI.

Keywords: Intracranial pressure; pulse pressure amplitude; compliance; volume-pressure response; hydrocephalus.

Introduction

The possibility of obtaining data about intracranial volume-pressure relationships has increased in recent years with the introduction of the bolus injection tests and the study of the CSF pulsatility. Volume-pressure studies producing rapid changes in the intracranial volume were introduced by Miller and Garibi[11] and Marmarou *et al.*[8, 9]. Later some authors pointed out that there are analogies between the CSF pulse wave and those rapid infusion tests, showing the pulse pressure amplitude, wave slope and morphology are related to the intracranial compliance[1, 3, 4, 10, 12, 15, 16].

It is clear that the information obtained by these studies could clarify further questions related to the pathogenesis and treatment of hydrocephalus and intracranial hypertension. However, since all intracranial volume-pressure studies require volume manipulations to the CSF spaces, clinical experiments involve a certain degree of risk and pose ethical and methodological dilemmas. On the contrary, laboratory studies using animal models allow unlimited research among homogeneous and controlled experimental groups. Avezaat *et al.*[1] studied all those volume-pressure responses in an acute experimental model of raised intracranial pressure by continuous inflation of an extradural balloon in dogs. The aim of our experimental work has been to study the volume-pressure relationships in a population of normal subjects and with subacute intracranial hypertension by using the animal model of kaolin induced hydrocephalus in dogs[5]. To achieve this, the bolus injection test proposed by Marmarou *et al.*[8, 9] has been performed both in normal animals and in those in the initial acute hypertensive stage of the model, followed by an analysis of the amplitude of the intraventricular CSF pulsations (AMP) and its relationships with the intracranial pressure (ICP), pressure-volume index (PVI) and intracranial compliance (C).

Experimental Materials and Methods

A total of fifteen adult mongrel dogs, averaging 15 kg in weight, were used in this experimental study. The animals were anaesthetized intravenously with sodium thiopental (10 mg/kg) and atropine (0.02 mg/kg) and mechanically ventilated. Systemic arterial pressure was monitored from a catheter placed into the femoral artery.

Dynamic volume-pressure studies of the intracranial spaces were undertaken following the placement of a catheter into the right lateral ventricle through a small burr-hole. First, baseline steady-state intraventricular fluid pressure (ICPo) and amplitude of the intraventricular pulse wave (AMPo) were measured. Afterwards, the bolus injection test as described by Marmarou *et al.*[8, 9] was carried out to study the volume-pressure relationships. The volumes injected varied from 0.05 to 0.5 ml of saline and were manually introduced intraventricularly via a three-way stopcock. The changes of the intracranial pressure during each volume manipulation were recorded

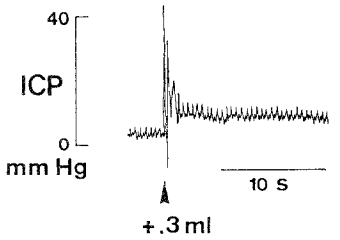

Fig. 1. Intraventricular pressure recording showing a bolus injection test in a kaolin-induced hydrocephalus dog

using a pressure transducer placed at the level of the cerebral ventricles and connected to the ventricular catheter. From the graph entries (Fig. 1) the Marmarou's pressure-volume index (PVI) and intracranial compliance (C) were calculated. The wave pulse amplitude was considered as the difference between the systolic and diastolic intraventricular pressure in a single pulse wave. The intracranial pressures were calculated from the diastolic plus a third of the pulse pressure. For calculations the measures were done in the centre of each respiratory cycle.

Calculations of PVI and C were computed according to the method of Marmarou *et al.*[8, 9]. The PVI, defined as the volume to be injected into the intracranial space to raise ten times the opening ICP, was calculated as follows:

$$PVI = V/10\, g_{10}\, (Pp/Po)\ (ml)$$

where V is the amount of fluid injected intraventricularly, Po is the baseline ICP and Pp is the peak ICP procuded by the bolus injection. Once PVI were obtained, the intracranial compliances were calculated as follows:

$$C = 0.4343\ PVI/P\ (ml/mmHg)$$

where P is the ICP.

Satisfactory experiments were achieved in five normal and seven hydrocephalic animals. Experimental hydrocephalus was induced by intracisternal injection of a sterile kaolin powder solution[5]. After the experiments were concluded animals were sacrificed and their brains removed and sectioned coronally for gross pathological examination. The experimental results obtained were statistically examined using the Student's t-test, linear and non-linear regression analysis and calculation of Pearson's correlation coefficient. The level of significance was chosen at p less than 0.05.

Results

Experimental data

The results of the experimental parameters are summarized in Table 1. Five animals were studied under normal conditions and seven were monitored an average of 15 days after intracisternal injection of kaolin. All injected animals had evidence of ventricular dilatation on postmortem examinations. Control group animals displayed a mean ICPo of 6.4 ± 1.5 mmHg and injected animals showed an state of intracranial hypertension with a significant increased of ICPo, showing a mean value of 22.8 ± 8.5 mmHg ($t = 3.92$, $p < 0.01$). There was also a significant increase of the AMPo, with a mean value of 1.0 ± 0.6 mmHg in normal dogs and of 5.0 ± 1.3 mmHg in injected animals ($t = 5.99$, $p < 0.001$). Volume-pressure responses during the bolus injection tests displayed a mean value of PVI of 0.24 ± 0.03 ml in normal animals and of 0.35 ± 0.20 ml in kaolin injected dogs ($t = 1.07$, p = ns) and a mean value in C of (17.6 ± 4.9) 10^{-3} ml/mmHg in normal group and (6.6 ± 1.9) 10^{-3} ml/mmHg in hydrocephalic animals, this difference being statistically significant ($p = 4.86$, $p < 0.001$).

Table 1. *Summary of Experimental Data Obtained in Normal and Hydrocephalic Animals**

Animal		ICP_o (mm Hg)	AMP_o	AMP_o/ICP_o	PVI (ml)	C. 10^{-3} (ml/mm Hg)
Normal	1	8.6	1.1	0.13	0.26	13.2
	2	6.5	0.6	0.09	0.28	18.8
	3	4	0.3	0.08	0.24	26.3
	4	6.7	2	0.30	0.19	12.4
	5	6	1.1	0.18	0.24	17.3
	mean ± SE	6.4 ± 1.5	1.0 ± 0.6	0.16 ± 0.08	0.24 ± 0.03	17.6 ± 4.9
Hydrocephalus	1	13.3	4.1	0.31	0.22	7
	2	23.3	7	0.30	0.37	6.9
	3	16.6	4.1	0.25	0.30	7.9
	4	26.7	5.3	0.20	0.27	4.3
	5	38.4	5.6	0.15	0.83	9.4
	6	28.3	6.2	0.22	0.23	7.4
	7	13.3	3	0.23	0.23	7.4
	mean ± SE	22.8 ± 8.5	5.0 ± 1.3	0.24 ± 0.06	0.35 ± 0.20	6.6 ± 1.9

* ICP_o: baseline intracranial pressure; AMF_o: baseline pulse amplitude; PVI: pressure-volume index; C: intracranial compliance; SE: standard error.

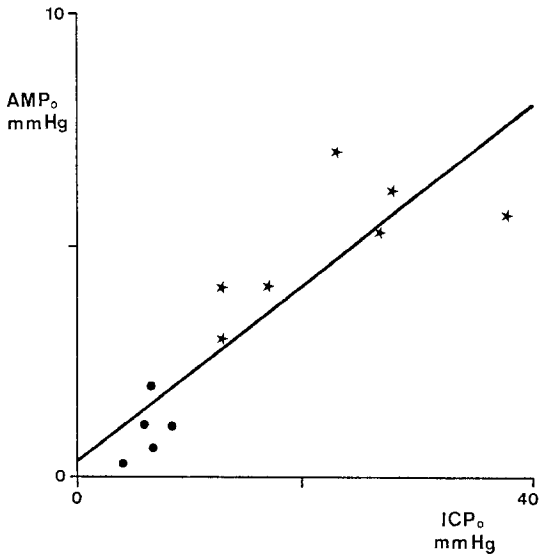

Fig. 2. Plot of the baseline intraventricular pulse amplitude (AMPo) versus baseline intracranial pressure (ICPo). The AMPo increases linearly with ICPo. The actual data from normal (●) and hydrocephalic (★) are printed. The equation of regression line is AMPo = 0.35 + 0.19 ICPo, and the correlation is highly significant ($r = 0.88$; $p < 0.001$)

Relationships between intracranial pressure (ICP) and pulse amplitude (AMP)

The ratio between AMPo and ICPo was calculated at baseline conditions (see Table 1). Its mean value in normal dogs was 0.16 ± 0.08 with no significant differences with injected animals, whose mean value was 0.24 ± 0.06 ($t = 1.94$, p = ns). A plot of ICPo versus AMPo is shown in Fig. 2 and a highly significant linear regression correlation was found when data from all animals were included ($r = 0.88$, $p < 0.001$). However, no significant results were obtained in regression analysis considering normal or hydrocephalus groups separately.

Relationships between intracranial pressure (ICP) and volume-pressure response

The plot of ICPo versus PVI from all animals showed a significant linear regression correlation ($r = 0.70$, $p < 0.05$) and is presented in Fig. 3 – left. There were no significant correlations when groups were plotted separately. The plot of ICPo versus C showed a highly non-linear (power regression) correlation ($r = -0.85$, $p < 0.01$) when data from all animals were included (Fig. 5 – left). This non-linear power regression correlation is maintained in control animals ($r = -0.85$, $p < 0.05$) but not in hydrocephalic animals.

Relationships between pulse pressure amplitude (AMP) and volume-pressure responses

Fig. 3 – right gives a plot of AMPo versus PVI from all animals and no linear nor non-linear correlations were found in regression analysis. The same results were

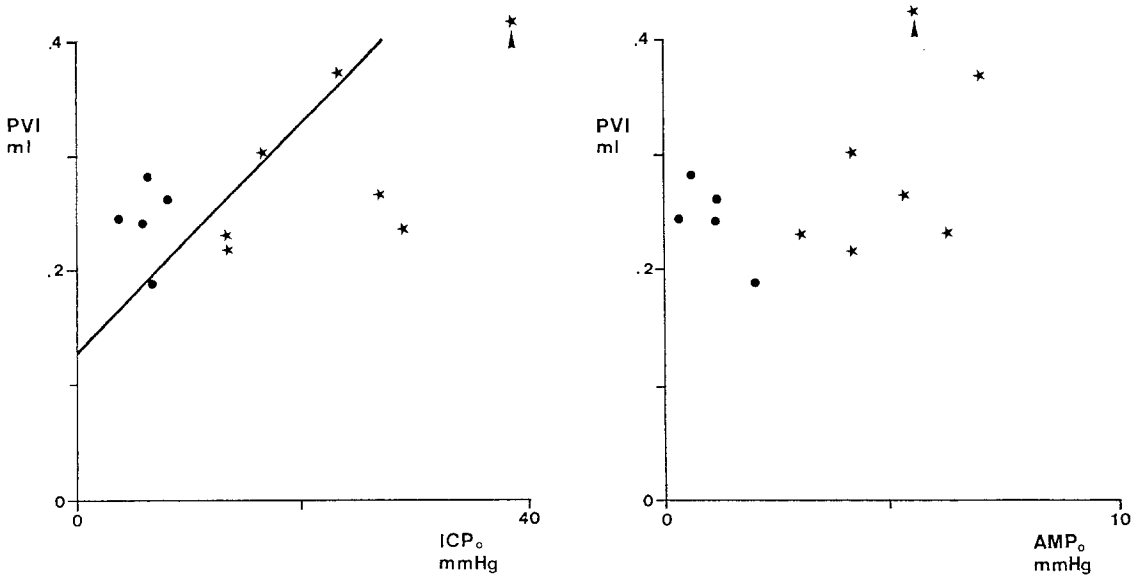

Fig. 3. Left: Plot of the pressure-volume index (PVI) versus baseline intracranial pressure (ICPo). The actual data from normal (●) and hydrocephalic (★) animals and the regression line are drawn. The equation of regression line is PVI = 0.13 + 0.01 ICPo and the correlation is significant ($p < 0.05$). Right: Plot of the pressure-volume index (PVI) versus baseline intraventricular pulse amplitude (AMPo). Data from normal (●) and hydrocephalic (★) animals are printed. No significant correlations were found in regression analysis

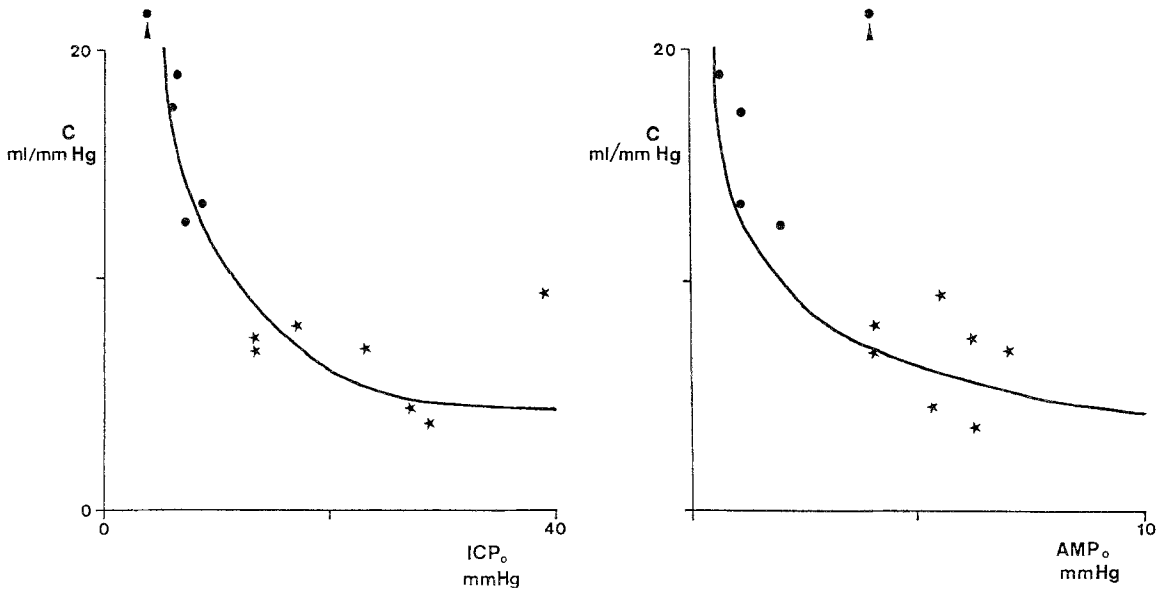

Fig. 4. Left: Plot of the intracranial compliance (C) versus baseline intracranial pressure (ICPo). A negative power correlation was found ($C = 56.47\ ICPo^{-0.70}$) when data from normal (●) and hydrocephalic (★) animals are computed. The correlation is highly significant ($r = -0.85$; $p < 0.01$). Right: Plot of the intracranial compliance (C) versus baseline intraventricular pulse amplitude (AMP) in normal (●) and hydrocephalic (★) animals. Regression analysis showed a negative power correlation ($C = 14.97\ AMPo^{-0.53}$) highly significant ($r = -0.90$; $p < 0.001$)

obtained computing separately each experimental group. Plotting AMPo versus C from all animals, a non linear (power regression) correlation was found ($r = -0.90$, $p < 0.001$). Fig. 4 – right shows the actual data and the regression curve. A similar power correlation was found plotting data from control animals ($r = -0.88$, $p < 0.05$), but did not from hydrocephalic ones.

Discussion

Studies of the intracranial volume-pressure relationships are based on injecting volumes into the intracranial space and recording the changes produced in the intracranial pressure. Recently, Marmarou *et al.*[8, 9] introduced a fast bolus injection test as an alternative to the more traditional continuous infusion tests and developed a non-linear mathematical model of the volume-pressure responses. This method allows a quick and safe determination of the pressure-volume index (PVI), which is a measure of the intracranial compliance (C), and the CSF absorption resistance.

The present experimental study was undertaken to examine the volume-pressure response in a population suffering a long standing intracranial hypertension. The main aim was to clarify the interrelationships among the intracranial pressure, CSF pulse amplitude and volume-pressure responses using the bolus injection test. An additional goal was to validate the bolus injection test as a useful method of assessing the volume-pressure response, mainly in order to predict from a single manipulation these responses.

The model of kaolin-induced hydrocephalus develops an initial phase of hypertensive ventriculomegaly accompanied, in relation to normal animals, by a reduction of intracranial compliance and an increase of pulse pressure amplitude. However, changes in PVI were not statistically significant in hydrocephalic animals, although the mean value of PVI was higher in these animals and PVI raised as ICPo did. As could be expected Tans and Poortvliet[17] and Shapiro and Marmarou[14] found a negative linear correlation between ICPo and PVI in patients with intracranial pathology. However, Shapiro *et al.*[13] found in hypertensive infantile hydrocephalus that PVI was significantly higher than in normal population and Kosteljanetz[7] did not find correlations between ICP and PVI in chronic communicating hydrocephalic patients. To explain this lack of correlation between ICPo and PVI in hydrocephalus, Shapiro *et al.*[13] have pointed out the ability of the dilated ventricles to store fluid without elevations of ICP buffering the volume-pressure response. On the other hand, although theoretically PVI reflects the volume-pressure response and the terms of PVI and intracranial C are interchangeables at a given ICP[8], it is not clear what the PVI represents. In opposition to those discussions we have found that the plot of ICP versus intracranial C offers a strong neg-

ative correlation as could be expected by the study of the mathematical formulas used to calculate PVI and C from ICP.

On the other hand, some authors have considered that the rapid entry of a sanguineous volume into the intracranial space during cardiac systoles would be a physiological bolus injection test. This has led to a study of the intracranial pulse wave form and its amplitude pressure, both in clinical and laboratory conditions[1, 3, 4, 10, 12, 15, 16]. In the genesis of the CSF waveform the pulsatile change of the total intracranial volume of blood was initially taken into consideration[2], the role of the biophysical conditions of the intracranial space has been considered expressed in terms of compliance or elastance[16] and, finally, factors directly related to the state of the intracranial vasculature have been implied[12]. Some authors have examined the possibility that each one of the above mentioned factors plays a role in the final morphology of the CSF pulse wave[3, 12]. However, considering only the pulse pressure amplitude, relations have been demonstrated between it and other parameters of the intracranial system[1, 6, 10, 15, 16]. As others have shown, we have found in our experimental study a direct linear correlation between ICP and AMP using data from all animals measured in the baseline steady-state. Since the AMPo/ICPo ratio is similar in normal and hydrocephalic animals it could be interpreted that the increase in pulse amplitude showed in hydrocephalic animals is solely the consequence of the baseline ICP augmentation. However, those AMP-ICP relationships in hydrocephalic animals could be explained by structural and biophysical changes of the hydrocephalic brain developing changes in intracranial compliance and consequently in the amplitude of the CSF wave. The relations shown in our study between pulse amplitude and intracranial compliance seem to support this hypothesis. However, we have found no correlations between pulse amplitude and PVI index. This fact would be explained considering that intracranial compliance reflects better than PVI the volume-pressure relations in the intracranial space.

Thus, we consider that pulse amplitude changes in acute hydrocephalus are related to intracranial compliance changes. Also we have shown[5] an augmentation in AMP with a nearly normal compliance in chronic normotensive kaolin-induced hydrocephalic dogs. However, in this late stage the main cause in the AMP increase would be the obstruction of the fourth ventricle outlets by the kaolin reactive fibrosis, leaving isolated the subarachnoid spaces which normally act as buffer for the intracranial pulse wave.

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