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How does CSF dynamics change after shunting?

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Objective – Hydrocephalus is much more complex than a simple disorder of cerebrospinal fluid (CSF) circulation. Shunting primarily corrects disturbed fluid flow which may have an impact on cerebral blood flow and metabolism. We studied hydrocephalic patients before and after shunting to characterize changes in their CSF compensatory parameters. *Material and methods* – We selected 25 patients and studied them retrospectively. All patients had ventriculomegaly and clinical symptoms of normal pressure hydrocephalus. After shunting, they were still presenting with some adverse symptoms, mainly headaches, slow improvement or no improvement of ventriculomegaly. Therefore, they underwent further infusion studies to assess shunt function. In all cases, the shunts were confirmed to be draining CSF adequately. Parameters of CSF dynamics: baseline intracranial pressure (ICP), resistance to CSF outflow, cerebrospinal elasticity, content of vasogenic pressure waves (pulse, respiratory and B waves) and compensatory reserve assessed as moving correlation coefficient between mean CSF pressure and pulse amplitude (RAP), were compared before and after shunting. *Results* – Mean ICP and resistance to CSF outflow decreased ($P < 0.003$) after shunting. All vasogenic pressure waves decreased ($P < 0.005$). Compensatory reserve (RAP) significantly improved ($P < 0.005$). *Conclusion* – A functioning shunt has an important impact on CSF circulation and pressure–volume compensation. Infusion studies can demonstrate the return of disturbed CSF dynamics to normal values even if clinical or radiological changes are not dramatic.

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Introduction

Hydrocephalus is commonly associated with disturbed cerebrospinal fluid (CSF) circulation (1, 2). However, little is known whether poor CSF circulatory reserve is always a primary cause of a disease. Many studies implicated specific disturbance in cerebral blood flow and its distribution (3, 4), decrease in brain metabolism (5), change in biochemical profile of CSF or brain tissue (6), etc. Nevertheless, CSF shunting was acclaimed to be a treatment of choice in communicating hydrocephalus. It is known that improving CSF dynamics by shunting leads to clinical improvement in 60–80% of normal pressure hydrocephalus (NPH) patients (7). There have been reports of improvement in regional CBF and oxygen metabolism rate after successful shunting (3). However, from the point of view of principles of shunt performance, it should be possible to measure the improvement in CSF dynamics after shunting. Previous studies (8–10) have attempted to highlight this problem. However, questions remain about the quantitative assessment of these changes, including influence of working shunt on CSF pressure vasogenic waveforms.

We retrospectively studied a selected group of patients with clinical/radiological diagnosis of NPH and with impaired CSF circulation and compared their compensatory parameters before and after shunting. The objective was to study which parameters of disturbed CSF dynamics

change after implantation of the hydrocephalus shunt. The observed values may serve as a useful gauge for shunt testing *in vivo*.

Materials and methods

CSF infusion studies are regularly undertaken as part of clinical assessment in our unit and a large database of studies has been accumulated [1992–2006, 1800 studies or cases of overnight intracranial pressure (ICP) monitoring, 980 individuals]. To address the question of quantitative change following shunting, we selected 25 patients (13 males and 12 females) with a mean age of 72 years (range: 45–84) and analyzed them retrospectively. This small number reflects the fact that most patients who undergo shunt surgery will not have a further infusion study unless they are being investigated for shunt malfunction.

Criteria for selection were as follows: clinical/radiological symptoms consistent with a diagnosis of NPH and appropriate infusion study profiles (i.e. normal CSF pressure and increased resistance to CSF outflow before the surgery). After shunting, some symptoms, such as persistent headaches, or sluggish improvement provoked the clinical query about shunt malfunction. These patients then underwent further infusion studies performed through the shunt pre-chamber. Patients were only included if there was no evidence of shunt blockage, partial obstruction or overdrainage.

All of 25 patients presented with clinical symptoms of NPH (gait disturbance 25, memory problems 15 and urinary incontinence 10) and global and communicating ventricular dilatation seen on MRI or CT scan. Eighteen patients were diagnosed with idiopathic NPH and seven patients with secondary NPH, thought to be due to previous subarachnoid haemorrhage or mild head trauma. All patients underwent shunt surgery. In 19 patients, a programmable valve was used. In the remaining patients, a fixed pressure (low or medium performance level) valve was inserted. The infusion test is part of the clinically accepted diagnostic pathway in our unit. Patients lie on an armchair in a semi-recumbent position for a minimum of half an hour before insertion of the needles. All tests are performed by infusing Hartman's solution into the ventricles (via an Ommaya reservoir or shunt pre-chamber). Two needles are inserted (25-gauge butterfly) and CSF is aspirated to confirm that the ventricular catheter is patent (not more than 1 ml). One needle is connected to a pressure transducer via a stiff saline-filled tube and the other to a syringe infusion pump. CSF pressure is monitored and recorded by a laptop personal computer running software ICM+ (http://www.neurosurg.cam.ac.uk/icmplus). After a minimum of 10 min of baseline measurement and when the patient's mean ICP is confirmed to be stable by computer analysis (no significant upwards or downwards drift of pressure), an infusion of normal saline at a rate of 1.5 ml/min was started and continued until a steady-state ICP plateau was achieved and maintained through a minimum of 10 min. The infusion is stopped prematurely if the ICP increases beyond 40–45 mm Hg as a safety precaution. The resistance to CSF outflow (Rcsf) is calculated as the difference between the mean value of plateau ICP and the mean value of baseline ICP divided by the infusion rate in cases when stable plateau was observed. In cases when ICP during the test increased above 40 mm Hg, Rcsf is calculated using mathematical matching of the modelling curve (1, 11) to the recorded pressure. In addition, the cerebrospinal elastance coefficient is calculated (E1, units [1/ml]) (11).

During the infusion study, the ICP waveform is continuously recorded and the analysis of ICP parameters is performed at baseline and during the infusion (plateau of ICP). The mean ICP is calculated, then the waveform is processed through a Fourier transform analysis to determine the pulse amplitude of ICP (AMP) as the peak-to-peak magnitude of the first harmonic component related to the heart rate. Slow waves (SLOW) were calculated as the power of frequency components between 0.05 and 0.0055 Hz. This is equivalent to the period from 20 s to 3 min – the range little bit wider than original 'Lundberg B waves' (30 s to 2 min). It is also important to emphasize that due to short period of observation in awake patients calculated 'SLOW' waves do not have the same meaning as 'Lundberg ICP B waves'. Magnitude of respiratory waves is expressed as the power of frequency components between 0.2 and 0.05 Hz.

The RAP index (correlation coefficient [R] between AMP amplitude [A] and mean pressure [P]) is derived by linear correlation between 40 consecutive, data points of AMP and time-averaged ICP acquired every 6 s. This index indicates the degree of correlation between AMP and mean ICP over short periods of time ($\sim$4 minutes). Its clinical significance has been discussed before (12). Theoretically, the RAP coefficient indicates the relationship between ICP and changes in volume of the intracerebral space, known as the 'pressure–volume curve' (13, 14). An RAP coefficient close to 0 indicates lack of synchronization between changes in AMP and mean ICP. This

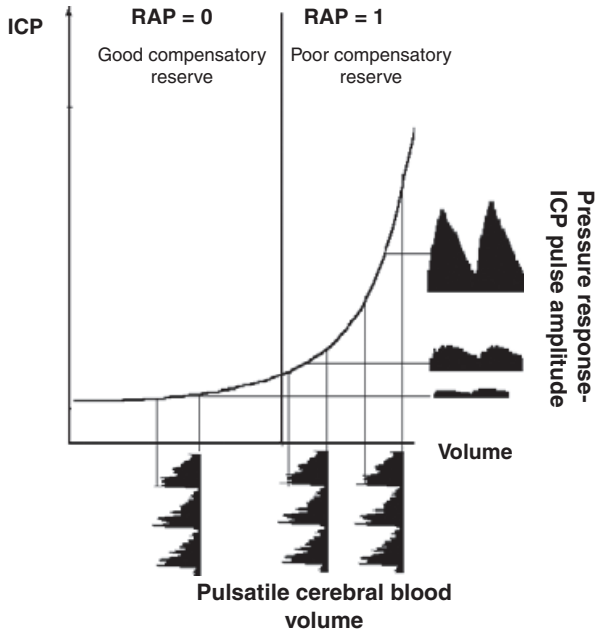

Figure 1. In a simple model, the pulse amplitude of ICP (expressed along the *y*-axis on the right side of the panel) results from the pulsatile changes in cerebral blood volume (expressed along the *x*-axis) transformed by the pressure–volume curve. This curve has two zones: a flat zone, expressing good compensatory reserve, and an exponential zone, depicting poor compensatory reserve. The pulse amplitude of ICP is low and does not depend on mean ICP in the first zone, resulting in values of RAP close to 0. The pulse amplitude increases linearly with mean ICP in the zone of poor compensatory reserve, resulting in RAP close to +1. Adopted from the data and models given in (13,14).

denotes a good pressure–volume compensation at low ICP (see Fig. 1). When RAP rises to +1, AMP varies directly with ICP and this indicates that the 'working point' of the intracranial space shifts to the right towards the steep part of the pressure–volume curve. Here, compensatory reserve is low; therefore, any further rise in volume may produce a rapid increase in ICP.

Plateau pressure measured during infusion study is compared with a value of so-called 'critical pressure' assessed in the laboratory (11) as: operating pressure (pressure across the valve perfused with water at a rate of 0.3 ml/min) of the valve plus hydrodynamic resistance of the opened valve times infusion rate.

Results

Examples of infusion tests performed in a typical patient before and after shunting are presented in Figs 2 and 3. Before shunting, the patient had normal baseline pressure with increased resistance to CSF outflow (the test was discontinued due to increase in a pressure close to safety limit of 40 mm Hg). After shunting, pressure was unchanged, but the resistance to CSF outflow was reduced.

Following shunting, gait improved in 21 patients whilst cognitive function improved in 14 patients. Thirteen patients were continued to complain of headaches. Detailed numerical results containing paired comparison of all 25 patients are presented in Table 1. Baseline mean CSF pressure, pulse amplitude and magnitude of slow vasogenic waves significantly decreased after shunting. Compensatory reserve expressed using RAP coefficient also improved. Calculated resistance to CSF outflow decreased. Plateau pressure achieved during the test correlated ($R = 0.81$; $P = 0.0001$) with a 'critical pressure' assessed for each particular shunt in the laboratory (see Fig. 4) (11).

Discussion

In all patients compensatory reserve and CSF circulation improved. Changes in parameters like baseline-, end-plateau-pressure and resistance to CSF outflow are obvious, as they are primarily taken as evidence of shunt functioning (15, 16). They have been described before (8–10). Decrease in pulse amplitude and magnitude of slow vasogenic waves are not so obvious; however, their decrease has been described before in observational studies (11). Generally, the shunt seems to have an impact on stabilization of CSF dynamics. Compensatory reserve seems to improve as well, although the elastance coefficient E1 did not suggest it. It is questionable, whether the interpretation of this coefficient after shunting is still valid as a functioning shunt introduces additional very strong non-linearity to the existing non-linear pressure–volume compensation curve (1, 13, 14).

Most of shunts have low hydrodynamic resistance (17) and large volumes of CSF may be drained from intracranial space relatively easily. These observations may be helpful in formulating criteria for interpretation of ICP monitoring in patients with shunt *in situ*. Such a monitoring is sometimes performed in cases when there is a suspicion of shunt blockage (18). ICP should be of low dynamics, indicating good compensatory reserve and pulse amplitude of the pressure waveform should be generally less than 2.5 mm Hg. Average ICP during the patient's sleep period should not be greater than shunt opening pressure increased by estimated value of abdominal pressure (5 mm Hg in slim patients but much greater in obese persons or pregnant women). ICP readings should generally not exceed 20 mm Hg over longer periods (longer than 2–3 min) with the exception of

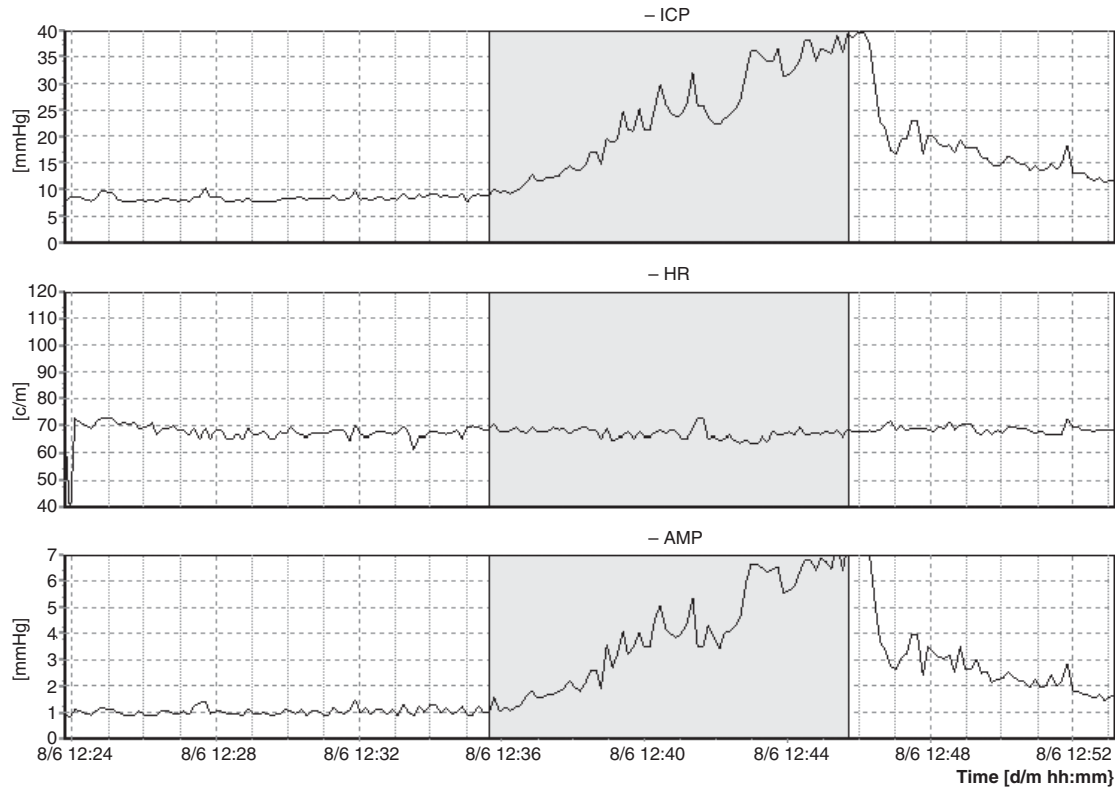

Figure 2. Example of infusion test performed before shunting. A 70-year-old lady with normal neurology except wide-based gait. Falls backwards, not associated with dizziness. Large ventricles, communicating hydrocephalus. Opening pressure was 8.4 mm Hg, infusion was discontinued at pressure 40 mm Hg., estimated resistance to CSF outflow was 23 mm Hg per ml/min. HR, heart rate. *x*-axis: time in format date hours:minutes.

slow vasogenic activation seen during REM periods of sleep (19).

Therefore, a functioning shunt seems to have an important impact on pressure–volume compensation. It is difficult to understand why these dramatic changes do not necessarily produce similar clinical results. It is possible that patients who complain of headaches in these situations are experiencing symptoms related to overdrainage (i.e. low pressure). However, none of the patients studied had slit ventricles or experienced dramatic changes in terms of ventriculomegaly.

We postulate that these patients may still be experiencing periods of overdrainage. Contemporary shunts are connected to valves which work like all-or-none devices (20). When these valves open, they can allow drainage of CSF through the shunt at a high rate. In some patients, there may be constant switching of valves between the on/off positions, i.e. from slight-overdrainage to slight-underdrainage state leaving the average ventricular volume almost unchanged. However, in intermittent periods, they may feel headaches related to abrupt changes in CSF volume. Only a few valves have hydrodynamic resistance (when open) above 4 mm Hg per ml/min, while physiological resistance varies from 6 to 10 mm Hg per ml/min (21). Siphon control devices (most of our patients had Strata valves equipped with such a device) do not always work without problems. Increased skin stiffness above the shunt is commonly implicated as a disturbing factor (22). If this is true, improvement in shunt technology may really be a factor with the potential to contribute to a better quality of life for patients with shunts. Continuous CSF drainage, independent of pressure gradients, matched to a CSF production rate will be an ultimate solution. It seems to be possible with an arrival of clinically feasible active valves (23).

Limitations

This is a study of highly-selected patients drawn from a large database (25 out of 1800). However, patients who undergo shunt surgery in our unit are not investigated with a further infusion study unless a specific query of shunt malfunction has been made. This is due to the risk of introducing infection into the closed shunt system. It is also theoretically possible to flush debris into the shunt tubing resulting in an inadvertent shunt blockage, Patients in whom the infusion study demonstrated a

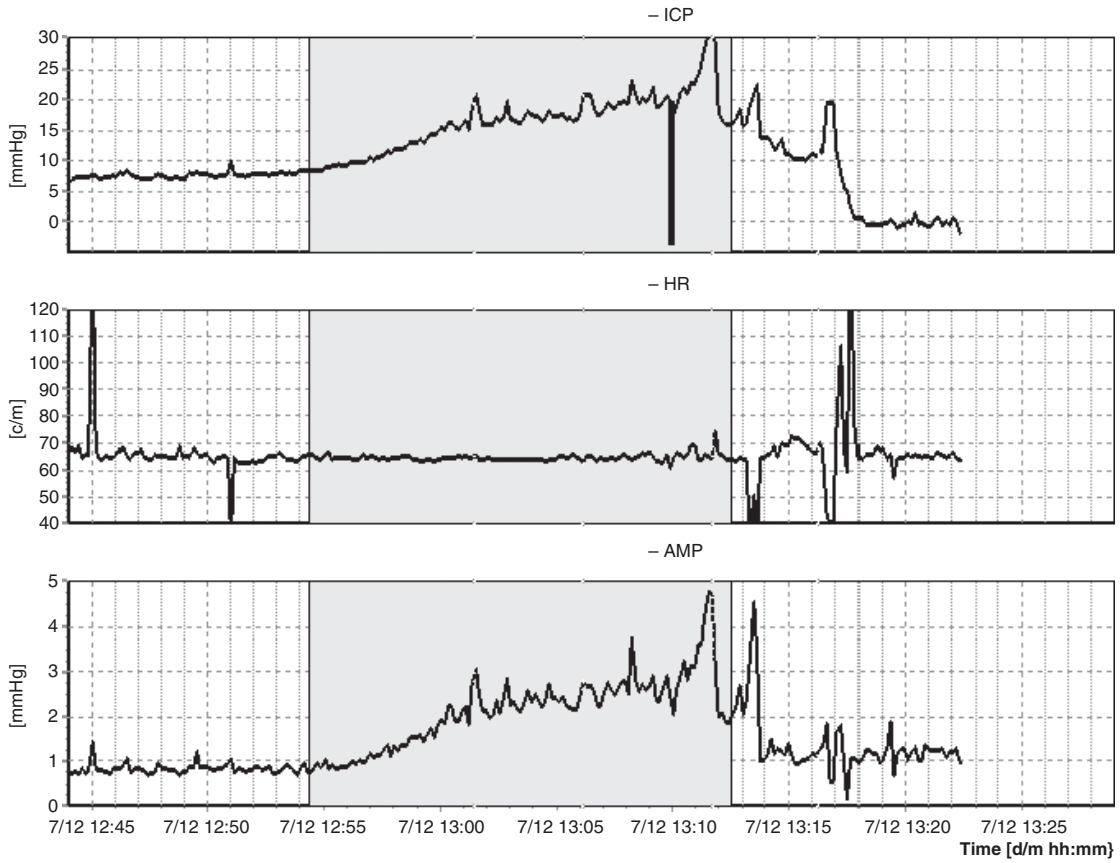

Figure 3. The same patient, test performed 5 months after shunting. Gait improved but several falls after shunting. Ventricles did not change. Opening pressure was 7.7 mm Hg, it increased to 17 mm Hg during the study. Resistance to CSF outflow was 6.1 mm Hg per ml/min. An additional test was performed at the end of infusion (marked as vertical black line on top plot). Flow through the shunt was blocked by compression of siphon-control device. Sharp increase in recorded pressure confirmed shunt patency.

Table 1 Median values and ranges of parameters calculated during infusion studies performed before and after shunting. P describes probability of null hypothesis using paired sign rank test

	Units	Before	After	*P*
ICP baseline	mm Hg	10.6 (–2.1 to 16.9)	6.0 (0.4–12.1)	0.00032
ICP plateau	mm Hg	35.0 (22.1–42.1)	15.5(5.8–22.7)	0.0000015
AMP baseline	mm Hg	2.5 (0.2–5.9)	1.4 (0.3–4.1)	0.0051
AMP plateau	mm Hg	8.1 (2.4–15.2)	2.7 (1.0–6.7)	0.0000015
RAP baseline		0.53 (–0.55 to 0.88)	0.27 (–0.63 to 0.90)	0.0051
RAP plateau		0.89 (0.73–0.99)	0.75 (0.40–0.99)	0.15
RESP baseline	mm Hg	0.37 ± 0.3	0.39 ± 0.38	NS (0.43)
RESP plateau	mm Hg	0.87 ± 0.68	0.52 ± 0.48	0.016
SLOW baseline	mm Hg	3.01 ± 2.23	0.56 ± 1.2	NS (0.42)
SLOW plateau	mm Hg	22.1 ± 21	3.07 ± 3.75	0.0051
Rcsf	mm Hg/(ml/min)	20.4 (13.1–28.9)	6.8 (2.6–10.7)	0.0000016
Elasticity	1/ml	0.21 (0.05–0.44)	0.21 (0.06–0.55)	NS (0.83)

ICP, intracranial pressure; AMP, pulse amplitude (first harmonic peak-to-peak) of ICP pulse wave; RAP, index of compensatory reserve; RESP, respiratory wave; SLOW, power of SLO waves; Rcsf, resistance to CSF outflow.

problem, for example a blockage, were not included. Therefore, the study is representative of the clinical patients we have assessed in our unit who are deemed suitable to fit the entry criteria into this study.

Patients were clinically assessed by the neurosurgical team in a prospective way but compensatory parameters before and after shunting were assessed retrospectively. It was not possible to classify the parameters of the infusion studies any further as they relied on clinical and radiological assessment made by different doctors and in different time-frames. The accuracy of some of

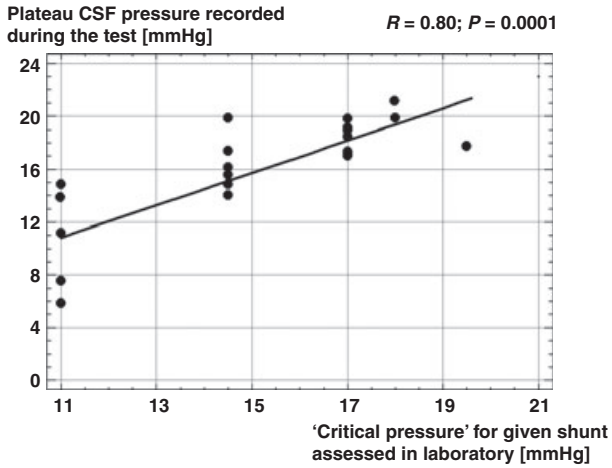

Figure 4. End-plateau pressure recorded during infusion tests vs critical pressure measured in the laboratory for a given type of shunt and its settings (12).

the parameters could be questioned – and this is almost always a case in retrospective analysis of NPH material.

We were unable to provide any general hypothesis that explains the discrepancy between clinico-radiological data and CSF dynamics findings in this series of patients. The answer may be found in a particular adjustment of each valve for each patient, a sort of individual 'fine-tuning'. It is our experience that programmable valves have greatly reduced the number of revisions due to minor complaints following shunting. This experience has been confirmed by many other worldwide centres in this field.

The findings we presented in this study are not surprising, but we feel they offer quantitative confirmation of the value of continuing to perform infusion studies in the clinical environment.

Conclusion

A functioning shunt has an important impact on CSF dynamics. Resistance to CSF outflow decreases, which is followed by a decrease in 'vasogenic components (pulse, respiratory and B waves)' of ICP waveform. However, confirmation of shunt function and quantitative evidence of the improvement of CSF dynamics may not be matched by dramatic clinical or radiological changes for the individual patient with a shunt.

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