LIKVOR

Shunt evaluation through infusion test

There is very strong evidence for using postoperative infusion test to investigate a suspected shunt dysfunction. Using this method will avoid many unnecessary shunt revisions and will help the clinician to adjust programmable shunts in a rational way. The purpose with this white paper is to describe how to evaluate an inserted shunt through a postoperative investigation of a patient's CSF system with the CELDA® System.

When a shunted Normal Pressure Hydrocephalus (NPH) patient deteriorates, it can be difficult for the clinician to differentiate between a progression of the disease and a dysfunction of the shunt system[1]. In an infusion test study comparing patients' cerebrospinal fluid (CSF) dynamics with a bench test investigation of CSF shunts, the results showed that the response in infusion studies is strongly influenced by the hydrodynamic properties of the shunt used. Since the patients have a normal pressure, the baseline pressure may be an unreliable index of shunt function while reduction in outflow resistance (R_{out}), being the inverse of the outflow conductance (C_{out}), in an infusion study provides reliable index of shunt function[2].

Various types of infusion tests

Four common infusion tests are used today to assess the CSF system characteristics, pressure levels, constant flow infusion, bolus infusion and constant pressure infusion. They differ in their use of infusion protocols and parameter estimation methods where the infusion can be either passive, with a pre-set infusion rate, or active, with pressure regulation via a controller. The former includes the constant infusion and bolus infusion protocols[1,3–9]. The active approach to the infusion test is used for the constant pressure infusion[10] and pressure levels protocol[11–15]. The latter uses elevated pressure levels, achieved via pressure regulation. All of these infusion tests are included in the Likvor CELDA® System, but the pressure levels protocol[12] is set as the standard protocol for a postoperative investigation.

Investigation of shunt functionality

There is very strong evidence for using a postoperative infusion test to investigate a suspected shunt dysfunction. Using this method will avoid many unnecessary shunt revisions and will help the clinician to adjust programmable shunts in a rational way. A large study with 197 shunted patients showed that *in vivo* shunt testing with infusion tests was easy, safe and clinically useful, and aid the decision in difficult clinical situations, where shunt malfunction is suspected but not certain[16].

It was also shown that infusion studies can demonstrate the return of disturbed CSF dynamics to normal values even if clinical or radiological changes are not dramatic[17]. Using a CELDA® prototype with the pressure levels protocol, it was shown that information about the patient's CSF dynamics, with and without a shunt, together with a detailed description of the shunt pressure and flow characteristics would give the physician easily interpreted results and valuable support in the shunt revision decision[13]. In another study, 32 patients with CSF shunts were evaluated with infusion tests before and after shunt surgery. The results showed that R_{out} was a reliable indicator of shunt function and of fundamental importance to distinguish a dysfunctional shunt from an aggravation of the primary condition in patients with communicating hydrocephalus[18]. A recent study used the CELDA® prototype and included pre- and postoperative infusion tests in 63 patients with a Medtronic Strata® shunt. The study showed that even for clinically improved patients, there is reason to perform a CSF shunt function test to further improve the clinical outcome and to exclude a possible placebo effect[14]. Using an infusion test to verify CSF shunt function, unnecessary shunt revisions may be avoided. The use of an adjustable CSF shunt should be accompanied by routines for follow-up that include adjustment and clinical response[14].

Likvor CELDA® System

The Likvor CELDA® System uses two pressure sensors to measure intracranial pressure (ICP) and a high-resolution peristaltic pump to perform accurate infusion of artificial CSF or drainage of CSF. These are built onto a sterile single use tube set that is connected to the patient by lumbar puncture. Solenoid valves control direction of CSF flow, through the sterile tube set, to or from the patient. CELDA® also carries a built-in laser allowing the instrument to be levelled to the patient, ensuring the accuracy of recorded pressures. In addition to built-in hardware alarm limits, the software also controls the incoming data, ensuring that investigations are performed in a safe and controlled way.
CELDA® can determine the patient's ICP at rest, and uses the infusion test to calculate the C_{out}[1].

Postal address
Likvor AB
90729 Umeå

Visiting address
Tvistevägen 47

Telephone
+46 90 19 05 17

Mail
Info@likvor.com

Org.nr
556726-7652

The infusion test can also be used to determine shunt functionality in patients that have already received a shunt[13,14]. In addition, CELDA® has two analysis protocols: preoperative and postoperative assessment of CSF dynamics. In both cases, the CELDA® Software calculates the mean ICP, the flow and the C_{out}, all in real time. For postoperative assessment of shunted patients, the siphon functionality is examined comparing ICP when lying down and sitting up.

Likvor CELDA® postoperative investigation

The postoperative investigation is used to assess CSF system dynamics[19] following shunt operation as well as for determining shunt function. The investigation is like that of the preoperative investigation. The CSF system is manipulated through the infusion and the corresponding pressure response is measured with the other needle. For the infusion tests used in CELDA®, it is a lumped parameter model of the CSF system that is used[4,6,10]. With the relationship between flow and pressure, and the mathematical model of the CSF system, the hydrodynamic properties can be characterized by estimating the system parameters[1]. A typical pressure response during a postoperative investigation is shown in Figure 1. Investigations using CELDA® are to be performed after prescription of a professional physician and by a trained operator. An examination using CELDA® begins by preparing the equipment, filling the accompanying disposable tube set (the CELDA® Tools), balancing and controlling the pressure sensors and registering patient details. Two needles are placed in the lumbar subarachnoid space, via lumbar puncture, thus connecting to the CSF system. One needle is used for infusion or withdrawal of Ringer solution (artificial CSF), the other for measuring the pressure. Tubes on the tube set are connected to the lumbar cannulas. If CSF samples are wanted, they are taken at this moment. The patient is placed in supine position, the instrument is levelled with the patient using the built-in laser, and the data gathering begins. If CSF has been removed, the same volume is restored to the system. Following this, the investigation starts with measurement of the baseline pressure. The infusion then starts and the pressure is regulated to six, consecutive levels lasting four minutes each. This will give a flow-pressure curve as shown in figures 2 and 3, where linear regression between flow and pressure provides an estimate of C_{out}[12]. Following the infusion is a relaxation phase lasting ten minutes where the pressure decreases towards baseline pressure.

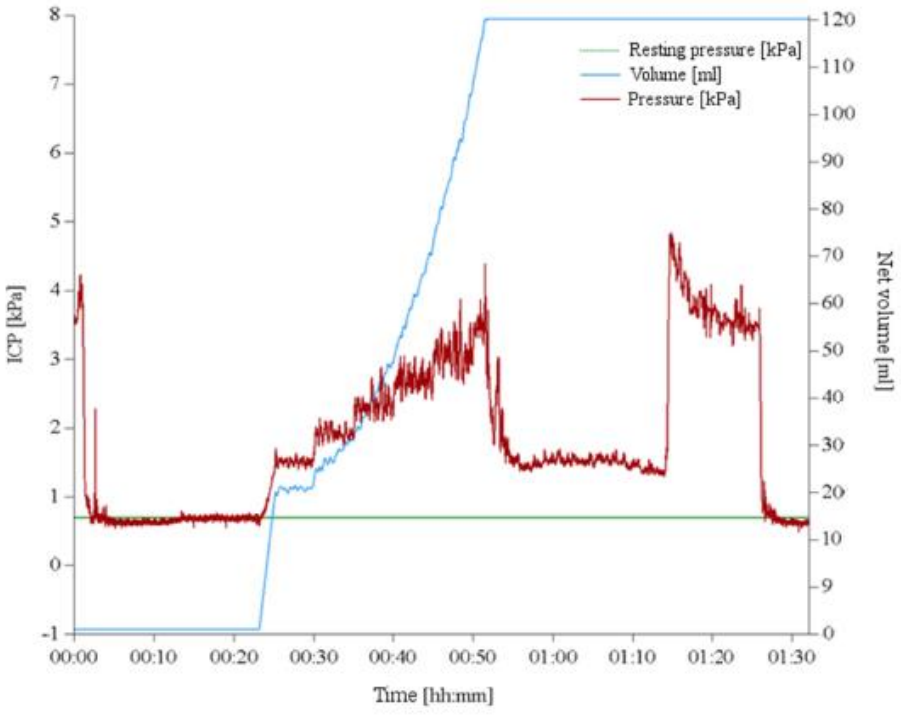

Figure 1. *A postoperative investigation where the pressure response is plotted over time (red line), with infused net volume of artificial fluid (blue line) and the measured baseline pressure (green line). The baseline pressure was measured during the first part of the investigation. Then came the infusion test with six pressure levels. The pressure relaxed toward baseline pressure and at the end an anti-siphoning test was performed.*

Results

Typical flow-pressure charts from postoperative investigations are shown in figures 2 and 3. These are from investigations on patients with pressure-regulated shunts (Strata®) obtained during postoperative investigations performed as a regular follow-up post shunt surgery. The high C_{out} values seen in figure 2 are indicating functioning shunts and the shape of the curve is typical for functioning pressure shunts where it is easily seen where the shunt is opening (at ~1.5 kPa). Apart from regular follow-up investigations, a major reason for performing the shunt test is to assess shunt function when there is a suspicion of a malfunctioning shunt. In figure 3, a typical example of a flow-pressure chart obtained during a postoperative investigation with a malfunctioning shunt is shown. The C_{out} value of 11 µl/s/kPa is below what is expected from a functioning shunt. The Likvor CELDA® System generates a pdf-file from the postoperative investigation. Results that are shown include baseline pressure, the C_{out} (=1/R_{out}) with (95%) confidence intervals, infused volume, and pressure before and after having been seated. The pressure during the entire investigation (figure 1) and a chart for pressure/flow (figures 2 and 3) are also presented.

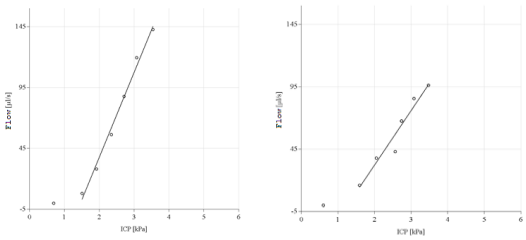

Figure 2. *Flow-pressure charts obtained during a postoperative investigation. The left figure gives a C_{out} of 70 µl/s/kPa and the right figure a C_{out} of 44 µl/s/kPa.*

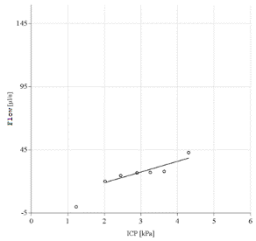

Figure 3. *Flow-pressure chart obtained during a postoperative investigation with a non-functioning shunt. The C_{out} is 11 µl/s/kPa.*

Discussion

A properly functional CSF system is of great importance. As knowledge of symptoms originating from a malfunctioning CSF system is continuously growing, the need for accurate and flexible tools to measure and describe CSF system conditions is becoming more and more important. The Likvor CELDA® System is a complete system for measuring CSF dynamics. The protocols in CELDA® cover the most common ways to investigate CSF dynamics without adding any new hazards. It is important that the produced estimates are reliable and can be interpreted accurately. An advantage of the infusion test is the objective assessment of the results, and that the results are independent on the performance of the patient and/or investigator.
CELDA® is not only unique as the first commercial instrument for better diagnostics of NPH but it is also a superior instrument for testing *in situ* shunt systems. Following a shunt implantation, follow-up visits necessary to evaluate whether unchanged or worsened symptoms can be corrected by shunt adjustment and to discover any cases of shunt dysfunction requiring surgical shunt revision[14]. Even improved patients could benefit with better adjustment of the shunt. In a pre- and postoperative evaluation with the automatic protocol it is easy to determine if a patient's shunt works as intended. Using the instrument in postoperative care can avoid many unnecessary operations and can optimize shunt functionality[14].
Investigations with CELDA® uses lumbar puncture to address the CSF system. Therefore, the practical and economical consequences are substantial. Lumbar puncture can be performed in an outpatient setting, where ventricular assessment necessitates hospitalization for 1-2 days including occupation of the neurosurgical theatre and post neurointensive monitoring. The Likvor CELDA® System is designed for assessment of CSF dynamics, and to allow multiple well-documented traditional examination methods to be performed with a single instrument in a controlled and safe way.

References

1. Eklund, A. *et al.* Assessment of cerebrospinal fluid outflow resistance. *Med. Biol. Eng. Comput.* **45,** 719–35 (2007).

2. Taylor, R., Czosnyka, Z., Czosnyka, M. & Pickard, J. D. A laboratory model of testing shunt performance after implantation. *Br. J. Neurosurg.* **16,** 30–5 (2002).

3. Katzman, R. & Hussey, F. A simple constant-infusion manometric test for measurement of CSF absorption. I. Rationale and method. *Neurology* **20,** 534–44 (1970).

4. Avezaat, C. J. & van Eijndhoven, J. H. Cerebrospinal Fluid Pulse Pressure and Craniospinal Dynamics. (1984).

5. Czosnyka, M. *et al.* A computer system for the identification of the cerebrospinal compensatory model. *Acta neurochirurgica* **105,** 112–6 (1990).

6. Marmarou, A., Shulman, K. & Rosende, R. M. A nonlinear analysis of the cerebrospinal fluid system and intracranial pressure dynamics. *J. Neurosurg.* **48,** 332–44 (1978).

7. Boon, a J. *et al.* Dutch normal-pressure hydrocephalus study: prediction of outcome after shunting by resistance to outflow of cerebrospinal fluid. *J. Neurosurg.* **87,** 687–93 (1997).

8. Malm, J. *et al.* Implementation of a new CSF dynamic device: A multicenter feasibility study in 562 patients. *Acta Neurol. Scand.* (2012). doi:10.1111/j.1600-0404.2011.01533.x

9. Marmarou, A. *et al.* Diagnosis and management of idiopathic normal-pressure hydrocephalus: a prospective study in 151 patients. *J. Neurosurg.* **102,** 987–97 (2005).

10. Andersson, K. Assessment of cerebrospinal fluid system dynamics Novel infusion protocol, mathematical modelling and parameter estimation for hydrocephalus investigations. *Umeå University Medical Dissertations* (Umeå University, 2011).

11. Ekstedt, J. CSF hydrodynamic studies in man. 1. Method of constant pressure CSF infusion. *J. Neurol. Neurosurg. Psychiatry* **40,** 105–19 (1977).

12. Andersson, N., Malm, J., Bäcklund, T. & Eklund, A. Assessment of cerebrospinal fluid outflow conductance using constant-pressure infusion--a method with real time estimation of reliability. *Physiol. Meas.* **26,** 1137–48 (2005).

13. Eklund, A., Lundkvist, B., Koskinen, L.-O. D. & Malm, J. Infusion technique can be used to distinguish between dysfunction of a hydrocephalus shunt system and a progressive dementia. *Med. Biol. Eng. Comput.* **42,** 644–9 (2004).

14. Lundkvist, B., Koskinen, L.-O. D., Birgander, R., Eklund, a & Malm, J. Cerebrospinal fluid dynamics and long-term survival of the Strata(®) valve in idiopathic normal pressure hydrocephalus. *Acta Neurol. Scand.* 1–7 (2010). doi:10.1111/j.1600-0404.2010.01432.x

15. Fridén, H. & Ekstedt, J. Instrumentation for cerebrospinal fluid hydrodynamic studies in man. *Med. Biol. Eng. Comput.* **20,** 167–180 (1982).

16. Petrella, G. *et al.* In vivo assessment of hydrocephalus shunt. *Acta Neurol. Scand.* **120,** 317–23 (2009).

17. Petrella, G., Czosnyka, M., Keong, N., Pickard, J. D. & Czosnyka, Z. How does CSF dynamics change after shunting? *Acta Neurol. Scand.* **118,** 182–8 (2008).

18. Malm, J., Lundkvist, B., Eklund, a, Koskinen, L.-O. D. & Kristensen, B. CSF outflow resistance as predictor of shunt function. A long-term study. *Acta Neurol. Scand.* **110,** 154–60 (2004).

19. Marmarou, A., Bergsneider, M., Klinge, P., Relkin, N. & Black, P. M. The value of supplemental prognostic tests for the preoperative assessment of idiopathic normal-pressure hydrocephalus. *Neurosurgery* **57,** S17–28; discussion ii–v (2005).