Implementation of a new CSF dynamic device: a multicenter feasibility study in 562 patients

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Objectives – The cerebrospinal fluid (CSF) infusion test is frequently used when selecting hydrocephalus patients for shunt surgery. Very little has been reported regarding adverse events. We present a prospective feasibility study.

Methods – Standardized devices for measuring CSF dynamics were built and 562 patients investigated: Needles were placed by lumbar puncture (LP). An automatic CSF infusion protocol was performed. Course of events during the investigation as well as adverse events were registered.

Results – Preoperative evaluation of normal-pressure hydrocephalus was the most common indication (63%), followed by evaluation of shunt function (23%) and intracranial pressure recordings (14%). The LP was successfully performed in all but nine cases with 24 patients (4.3%) reporting major discomfort. Ringer infusion was performed in 474 investigations, and a valid measurement of the outflow resistance was received in 439 (93%). During the infusion phase, 17 (4%) patients reported severe headache. Infusion volume was significantly higher in patients having subjective symptoms during the infusion phase compared with those without adverse events. During 269 preoperative CSF tap tests, six (2%) patients had severe headache. Post-investigational headache was reported by 83 (15%) patients at the 24-h follow-up. No serious adverse events were observed. Conclusion – Infusion testing was safe and without serious adverse events with a high rate of successful procedures. The investigation was associated with expected mild to moderate discomfort.

Introduction

Pressure, flow, and volume of the intracranial cavity as well as their relationships define the cerebrospinal fluid (CSF) dynamic system. A disturbed, unbalanced system is seen in several neurological conditions such as hydrocephalus, idiopathic intracranial hypertension, and traumatic brain injury (1). In selecting CSF shunt candidates among patients with signs suggesting normal-pressure hydrocephalus (NPH), predictive or supplementary CSF dynamic tests are used (2). Although non-invasive predictive tests are desirable (3), the most common tests today are invasive, such as intracranial pressure (ICP) monitoring, 3-day external lumbar drainage (ELD), CSF tap test (50 ml), or the infusion test. Little is known about complications because of these tests. Serious adverse events caused by the predictive test should be added to the surgical risk and the risk by the shunt itself, when reporting outcome of shunt surgery. To evaluate the rate of rare but serious complications, studies including large patient cohorts have to be performed.

CSF infusion methods are used to study the pressure and flow of the CSF dynamic system. Usually, two needles are applied in the lumbar CSF sac. One needle is used to record pressure and
the other to infuse or drain Ringer solution. The most common parameters obtained are ICP, resistance to CSF outflow (Rout), pulse pressure amplitude, CSF production rate, and the compliance of the system.

At the Umeå University Hospital, a CSF dynamic device has been developed and used in-house (4). Replicas of this device were built, and in August 2007, the equipment began to be used at four other Scandinavian university hospitals.

When new technical equipment is introduced, new staff have to learn how to operate the device. This implicates a potential risk of increasing the complications and that the indications for the investigation drift or change over time. The most common side effects regarding infusion methods are probably caused by the lumbar puncture (LP). Transient radiating pain and postdural puncture headache may be common complaints. During the investigation, a Ringer solution is infused, but very little is known about its interaction with the brain or side effects caused by the induced increase of ICP. No prospective feasibility study investigating a large patient cohort with an infusion test has previously been published.

The objective of this paper was to perform a large prospective multicenter feasibility study regarding the implementation of a new, highly standardized CSF dynamic device at five university hospitals.

Method and materials

The university hospitals in Uppsala, Linköping, Göteborg, Umeå (Sweden) and Aalborg (Denmark) participated in the study. In 2007, the CSF dynamic device was installed at each center, which approved to include the first 100 patients investigated at each hospital. The study period ended at the beginning of 2009, and 562 investigations were performed.

Indications for the investigation as well as side effects were registered. Variables describing the LP, the infusion of Ringer solution, and the CSF tap test were recorded. Complications during and 24 h following the test and the patient’s experience of the investigation were obtained. Patients with persistent radiating pain at the 24-h investigation were followed by a phone call or verification from the referring physician.

At the end of each investigation, the operator had to fill in a computerized case record form (CRF) to be able to end the investigation thus 100% data compliance was secured regarding the CSF dynamic investigation. The percentage of answers at the 24-h follow-up was 92%. The CRF file was anonymized (regarding name, sex and age), exported, and compiled to a database at Umeå University.

The study was approved by the Internal Review Board at Umeå University.

The Umeå CSF dynamic device

In Umeå, the history of using CSF dynamic tests and developing infusion devices is long. The fourth generation was introduced in Umeå in 2004, and failure mode analysis was performed according to the failure mode, effects, and criticality analysis (FMECA) standard (5). The technical features of the device, the test re-test reliability, and accuracy have been thoroughly investigated and validated on a patient population as well as on a standardized in vitro CSF dynamic model (3). As a means of conforming and improving the CSF infusion test also at other centers, four more CSF dynamic devices were built as replicas of the first one to be used at the University Hospitals in Uppsala, Linköping, Göteborg and Aalborg.

The CSF dynamic device was PC-based and the electronic control unit included analog safety checks that stopped the pump at dangerously high or low ICP. Communication between the electronic unit and the software was ensured by the use of an alternating signal, and a horizontal laser line enabled zero level alignment of the device in relation to the patient. Two pressure transducers connected to separate LP needles enabled continuous pressure recording as well as immediate feedback if one transducer stopped functioning. Investigation protocols and analyses were fully automatic as to obtain standardized and objective output parameters.

A custom made bed with a rectangular hole at the lumbar level allowed investigation in the supine position using two lumbar needles (1.2 mm, 18 G) connected to a computer using specially designed software controlling the system (Fig. 1). The investigation procedure was fully automated and standardized. Protocols for either a prolonged pressure recording (30 min), a constant pressure, constant flow or bolus infusion as well as a CSF tap test were available and could also be combined. The constant-pressure protocol was recommended as a first choice, as it included a real-time estimation of the Rout reliability (4). A written report was automatically generated immediately after the investigation.

Introduction at each center

A 4-day course was given to all nurses involved in operating the CSF dynamic device. The course
included theory, simulation of various situations in a bench test, participation during one patient investigation as well as to conduct one investigation under the supervision of an experienced instructor. A similar scheme was used for the physicians, but for 2 days. At delivery of the CSF dynamic device, the first investigations were supervised by an instructor to ensure proper handling.

Results

In May 2009, 563 patients had been included in the study. During local anesthesia, one patient had presyncope and the investigation was disrupted without any LP attempt. Thus, the study population consists of 562 patients. Two hospitals investigated 29% of the patients each, two hospitals about 16% each, and the fifth hospital investigated 9% of the patients.

The investigation was performed preoperatively as a diagnostic aid for suspected NPH in 353 (63%) patients. Another 129 (23%) were investigated following CSF shunt operation to assess shunt function, and 80 (14%) examinations were plain recordings of ICP, mainly performed on the indication of headache or idiopathic intracranial hypertension.

The lumbar puncture

The LP could not be successfully performed in nine of 562 cases (1.6%) (Fig. 2). In five of these, one of the two needles could be placed, and a planned infusion protocol was switched to registration of ICP. In the other four, there were no access to the lumbar space and the investigation was canceled.

In 32 (6%) of the successful LPs, the dura was penetrated more than once with one needle, producing risk of leakage and therefore jeopardizing the results of the investigation. During LP, 429 patients (76%) reported no or mild discomfort. In 128 patients (23%), transient radiating pain was noted and nine patients (1.6%) had moderate or severe pain. None of the latter nine had syncope. Nine patients (1.6%) suffered from severe dizziness, nausea or pallor during the LP, and another six (1.1%) had a syncope. In total, 24 patients (4.3%) experienced major discomfort during LP (severe pain, presyncope or syncope).

The infusion protocol

Infusion of Ringer solution was performed in 474 (84%) of the 562 investigations. The constant-pressure protocol was primarily chosen by the operator in 444 (94%) of the investigations, and a constant flow protocol in the remaining. The constant-pressure protocol was interrupted in 78 of 444 cases (18%). The reason for this was partial or total needle obstruction in 67 cases and other causes in 11 cases. In 44 (56%) of these interrupted investigations, the constant-pressure protocol was switched to constant flow, and in the remaining, the infusion test was terminated. Altogether, a valid measurement of the outflow resistance was received in 439 of 474 investigations (93%). For these investigations, a mean $\pm$ SD of 50 $\pm$ 24 ml ($n = 319$) Ringer solution was infused in the preoperative infusion tests and 77 $\pm$ 44 ml ($n = 120$) when shunt function was tested.
During the infusion phase, 394 of the 474 patients (83%) reported no discomfort. Sixty-one (13%) of the patients experienced a mild headache, dizziness, or nausea. A severe headache was reported in 17 (4%) cases, of whom three also experienced a presyncope. Another patient had presyncope without any headache, and one patient had syncope. Figure 3 displays subjective symptoms divided into pre- and postoperative investigations.

Among the patients with successful estimation of CSF outflow resistance, the infusion volume was significantly higher in the group having subjective symptoms during the infusion phase compared with those without symptoms $[75 \pm 43$ and $54 \pm 29$ ml, respectively ($t$-test $p < 0.001$)] (Fig. 4).

In 269 of 353 preoperative infusion tests (76%), a tap test removal of $38.3 \pm 10$ ml CSF (mean ± SD) for predictive purposes ended the infusion test. Six (2%) of these patients suffered from a severe headache during the CSF tap.

Adverse events 24 h after the investigation

No side effects were reported in 422 (75%) cases 24 h following the infusion test. Another 83 (15%) patients had headache, and 74 (13%) complained of back pain. Of the 83 patients with postinvestigational headache, 16 had only an ICP recording (i.e. one needle). Among the 128 (23%) patients experiencing short-lasting radiating pain at the LP, only six reported radiating symptoms at the 24-h follow-up and in all cases the symptoms disappeared within days.

Discussion

This is the largest study carried out using a lumbar infusion technique for investigation of the CSF dynamic system, and one of the first feasibility studies of invasive supplementary tests used in the investigation of hydrocephalus patients. The standardized CSF dynamic device as well as automatic investigation protocol provided flexibility and a high rate of successful investigations. Investigational problems were primarily related to the LP and to obtain a free flow through the lumbar needles. The investigation was associated with expected mild to moderate discomfort. Afterwards, positional headache was the most common complaint. No serious or permanent adverse events were observed.

The apparatus and indications for use

Prior to the study, all centers had extensive experience performing the 50 ml tap test. Four of the five centers also had in-house developed equipments for infusion tests. The introduction program for the new equipment including theory and ‘hands-on’ activities for both nurses and physicians worked well, and there were few operational disturbances requiring external support during the study period. Based on the current study, three important indications for infusion tests emerged:

1. Preoperative examination of patients with suspected or possible NPH,
2. Postoperative investigation of the patency of CSF shunts,
3. Lumbar pressure measurement in patients with suspicion of raised ICP.

On the indications of preoperative investigation or test of shunt patency, the use of a constant-pressure infusion protocol was recommended. The main reason for this was the simultaneous
calculation of a 95% confidence interval of the estimated resistance to CSF outflow (Rout) that was only provided within these protocols. This allowed the investigator to assess the reliability of Rout in real time and thus take proper action if the reliability of the measurement was high enough or too low. Another reason for using constant-pressure infusion was the visually appealing pressure/flow chart (4). This was especially useful when investigating shunt function because the character of the shunt, including shunt opening pressure compared with patient resting pressure as well as partial occlusion of the shunt, could be deduced from it.

A drawback with the constant-pressure infusion protocol was that partial or total needle obstruction in some cases made it impossible to withdraw CSF and thus complete the protocol. Most commonly, these problems appeared the first time the pump withdraw CSF, and the protocol could then be switched to constant flow infusion. When this switch of method was not made, it was sometimes because of the general state of the patient, but it was especially frequent when the investigators were new to the investigation procedure. This emphasizes the need of thorough introductory training. In a recently published study, it was shown that there was no significant difference in Rout as assessed by the constant-pressure infusion protocol as compared with the constant flow infusion protocol (6).

When idiopathic intracranial hypertension is suspected or on the indication of headache, the most common way of measuring ICP is by using a graded spinal fluid manometer with estimation of the height of the CSF column. This kind of measurement gives only one instant value of ICP, and the result is subjected to errors (7). In this study, the use of a 30-min ICP measurement offered the possibility to look at not only mean ICP of the patient but also the arterial pulsation amplitude and slow waves (i.e. B-waves) (8, 9). Also a more reliable mean pressure was found once ICP had stabilized during 30 min.

Adverse events for simultaneous infusion and tap tests

Almost all LPs were successfully performed, with or without corrections of the needles (Fig. 2). This may reflect the experience of the investigators, but also that the LP was performed in a sitting position (10). In a few patients, the dura was penetrated more than once. In such a case, a CSF leakage resulting in secondary measurement error may be avoided if the investigator instead of removing the malfunctioning needle reinserts the stylet and then places a new needle in parallel to the old one.

In previous studies, the frequency of post-LP headache varies between 1% and 30% (11). This corresponds well with the frequency of 15% found in this study. We only registered complications 24 h after the investigation, and it is well known that the post-LP headache can start several weeks after the LP. Thus, our figures should probably be somewhat higher. Atraumatic needles, smaller needle diameter, and insertion of stylet before needle removal have all been described to decrease the prevalence of post-LP headache dramatically (11). The large diameter of the infusion needles in this study (1.2 mm; 18G) has actively been chosen to give a negligible resistance that is important for the reliability of the results (12). An improvement to simplify the procedure, and probably decrease the headache frequency, would be a two-channel needle system, making one of the two needles used today redundant. Radiating pain is common at LP, but is usually very short-lasting as seen in this study.

During the infusion phase, many patients experienced mild headache, dizziness or nausea, but surprisingly few had severe complaints. The amount of Ringer solution infused is dependent on how much the ICP is increased, the patient’s outflow resistance as well as the duration of infusion. From our results, it seems likely that the amount of Ringer solution infused is related to these symptoms (Fig. 4). The physiological effects induced on the CSF dynamic system by the Ringer solution and the artificial ICP rise, as well as their effects on the measurement parameters, are unknown (13). Further, nausea was mainly experienced during the infusion phase, indicating that this might be connected to a large infusion volume or a high ICP. The frequency of subjective symptoms was also higher in the shunted patients where the infusion volume was larger (Fig. 3). The incidence of positional headache was about the same in the group of patients going through a complete infusion test compared with those only registering ICP. This indicates that the infused volume does not increase the risk of post-punctural headache. The drain phase (i.e. ‘the 40–50 ml tap test’) seems to be well tolerated by the patients, and the reported headache frequency was about the same as during the infusion phase. An interesting observation was that the patients reporting headache during the infusion phase were not the same as those reporting headache during the CSF drainage.

Infusion test compared with other invasive supplementary tests

The risks of invasive tests in hydrocephalus investigations should preferably be reported and incorporated in the final shunt surgery results. We
believe that all tests should be evaluated and the spectra of complications clarified in a study similar to the present before becoming a standard supplementary test. It has been shown that mean ICP is the same in the brain as in the lumbar space, but also that the cardiac pulsations are similar (14). A lumbar infusion test seems to be an easier and cheaper option compared with the intracranial registration of ICP, presumably with less adverse events. A recent study described about 0.5% serious complications or death after ICP monitoring(15).

The ELD test is becoming increasingly popular, especially in the US(10, 13, 16). A catheter is applied in the lumbar sac, and CSF is drained continuously or at regular intervals for several days. Serious adverse events, such as meningitis and subdural hematoma, have been described (10, 13, 16). In a recently performed feasibility study on 233 patients undergoing the ELD test (10), complications were noted in 19 cases (8.2%), of which 12 (5%) were considered minor and seven (3%) were deemed to be significant (two meningitis, one retained catheter, four symptomatic intracranial hemorrhages).

The use of reliable predictive tests to determine candidates suitable for shunt surgery is an important issue to ensure that a larger amount of those benefitting from it will receive treatment (17). There is no consensus regarding Rout as a supplementary or predictive test for outcome of shunt surgery in NPH (2). Studies are both positive (18) and negative (19) but the test is still recommended in the NPH guidelines (2). However, variation in results can partly be explained by the use of different techniques with various accuracy. The method used in this study has previously been validated (4), and we consider it suitable for prospective studies.

Infusion tests are today the only method to describe the CSF dynamic system in humans with simultaneous recording of pressure and flow. No serious adverse events were observed in this study, and we conclude that the infusion technology including the tap test is a safe procedure. The infusion technique allows shunt function to be evaluated postoperatively with low risk of complications. ICP can be measured with high accuracy.

Acknowledgements
This project was funded by the Swedish Research Council, Vinnova, and the Foundation for Strategic Research through their joint initiative Biomedical Engineering for Better Health.

Conflict of interest
See “financial disclosure”.

Financial disclosure
Jan Malm has received personal compensation from Medtronic Corporation for consulting and has received a royalty from Likvor AB. Anders Eklund has received personal compensation from Medtronic Corporation and Codman Inc for consulting and has received a royalty from Likvor AB. Nina Sundström has received a royalty from Likvor AB. In 2008, she was an employee for Likvor AB.

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