Neurosurgical forum
Letters to the editor

Poor Prognosis/Good Outcome in Patients with NPH


Abstract

Object. The authors set out to describe the outcome in a subgroup of patients with normal-pressure hydrocephalus (NPH) in whom prognostic factors were poor. This subgroup of patients who had received shunts was selected according to strict criteria.

Methods. From a cohort of 56 patients with NPH in whom shunts were placed, the authors selected a subgroup with four of the factors traditionally considered to indicate poor prognosis: idiopathic type, cortical atrophy, longstanding symptoms, and presence of dementia in addition to old age. Twelve patients met the inclusion criteria.

After receiving shunts, 92% of the patients showed clinical improvement on the NPH scale: gait improved in 100% of patients, sphincter control in 90%, and dementia in 33%. Improvement was significant for gait and sphincter control, general NPH score, and most daily life activity scales. No significant differences regarding clinical, cognitive, or functional changes following surgery were found in comparison with the rest of patients (the good prognosis subgroup).

Conclusions. The clinical condition of patients with NPH who present with traditionally accepted markers of poor prognosis can improve after surgery, especially as regards gait and sphincter control. The authors assert that the presence of these markers should not be considered to be an absolute criterion for ruling out shunt surgery in cases of NPH syndrome.

This letter concerns the authors’ second factor indicative of poor prognosis, cortical atrophy and its delineation. The computerized tomography (CT) scans presented in Fig. 3 of their paper were obtained in a patient who was presumed to have dilated cortical sulci (taken to indicate cortical atrophy) and who, against the odds, responded favorably to a shunt placement. Yet these scans demonstrate widening of the Sylvian fissures and the cerebral sulci at the midlevel of the cerebral convexities, in addition to that of the periventricular lucencies. No uppermost CT scan cuts are shown. In my study,2 I described the presence of obliteration of the cerebral sulci in the uppermost CT scan cuts and dilation of the subarachnoid spaces at lower levels, including the Sylvian fissures, in patients with NPH. The finding was considered to indicate obstruction of the subarachnoid spaces of the convexity of the hemispheres with subsequent dilation of all the spaces below the level of obstruction. In Fig. 3 of my paper I presented CT scans obtained in a patient with NPH that showed dilation of the Sylvian fissures in addition to marked ventricular enlargement. He responded well to treatment, and both the ventricles and the Sylvian fissures diminished in size postoperatively. This pattern was also documented in the two patients described by Salibi, et al.,1 and is also shown in the postoperative scans of the patient presented in Fig. 3 by Poca and colleagues. Figure 2 of their paper refers to a patient with NPH. The legend reads “despite enlarged Sylvian fissures and cortical sulci, the patient demonstrated intracranial hypertension on the ICP [intracranial pressure] tracing, with 51% of high-amplitude B waves.” I presume that the authors use this case as an example of a patient with NPH and cortical atrophy who despite the latter has intracranial hypertension. If this assumption is correct, then I believe that their statement is misguided and misleading. Unless the authors can demonstrate widening of the cerebral sulci in the uppermost CT scan cuts, the patient should not be considered to have cortical atrophy. Widening of the subarachnoid spaces at the midlevel of the hemispheres and that of the Sylvian fissures mostly probably follows obstruction of the subarachnoid spaces high in the convexity of the hemispheres. The pathological substrate of this obstruction is unknown, but possibly it is attributable to compression and obliteration of the spaces by the expanding ventricles.

This feature should not be considered a bad prognostic criterion in patients with the syndrome. It certainly should not be confused with cortical atrophy.

J. Vassilouthis, M.D.
Athens Medical Center
Athens, Greece

References


Response: We thank Dr. Vassilouthis for his letter. We are aware of his studies in the field of NPH1 and appreciate his interest in and comments on our work. His letter provides us with the opportunity to broaden discussion of the still-controversial topic of the real significance of increased cortical sulci size in patients with NPH and to explain the actual ICP values that these patients may have in further detail.

Dr. Vassilouthis’ comments focus on the patient whose CT scan is shown in Fig. 3 of our article. As Dr. Vassilouthis correctly points out, this scan shows a widening of the Sylvian fissures and the cerebral sulci at the midlevel of the cerebral convexities in addition to that of periventricular lucencies. For the sake of space and clarity, only two CT scan slices were included; the figure was chosen not to discuss whether or not the cortical sulci were dilated but to show how a patient with moderate ventricular dilation only and widened cortical sulci can have NPH and improve after shunt insertion. The uppermost slices are shown in Fig. 1 of this letter. We believe that after seeing this figure, Dr. Vassilouthis will agree that the cortical sulci are not obliterated in them and therefore that our point is clinically relevant and not “misleading and misleading.”

In all patients with suspected NPH, we analyze the sulci size at different levels, as well as Sylvian fissure size.1 In our study, we used cortical sulci size as inclusion criteria, not
sylvian fissure size; however, in all 12 patients, the size of all these structures increased simultaneously. We believe that this is evident in Fig. 2 of our article, which shows extreme enlargement of some cortical sulci. Cortical sulci enlargement are also evident in one of the slices of the presurgical CT scan shown in Fig. 3 (upper right) of our article, and is even more obvious in Fig. 1 of this letter, which shows the patient’s complete set of magnetic resonance imaging slices. Both figures provide evidence that the patients included in our study had cortical atrophy.

Figure 2 of our paper was chosen to emphasize that patients with what is still known as NPH can have intracranial hypertension even when cortical atrophy is evident. This phenomenon has been mentioned by several authors and we described it extensively in 1991 in a paper published in Acta Neurochirurgica (Wien) in which the following comment was added by the editor, “The authors decided—against suggestions of our reviewers—to include patients into their study who had higher than normal ICP values and therefore cannot be considered to suffer from NPH. The argument of the authors has been, that they presented only patients with typical clinical syndromes. With some reluctance we finally have accepted the paper as it stands. But we still are convinced that it would have been better to include only patients into this interesting study who really belong to the Normal Pressure Hydrocephalus group.”

After this paper was published, and after the increased use of continuous ICP monitoring in this syndrome, this phenomenon was also reported independently by other authors. Evidence is accumulating that in some patients with NPH syndrome, mean ICP is not always normal, even when these patients have no symptoms of intracranial hypertension but show the classical symptoms of the NPH syndrome. In some of these patients, continuous ICP monitoring shows either isolated episodes of intracranial hypertension (usually during rapid eye movement sleep) or continuously elevated mean ICP. Although the term “normal-pressure hydrocephalus” as first described by Hakim continues to be used, the alternative term “adult chronic hydrocephalus” (which does not indicate ICP value or any physiopathological theory) is being increasingly adopted and better defines this complex and frequently encountered syndrome.

The association of marked sylvian fissure enlargement and obliterated cortical sulci in some patients is well known. Data from recent studies have revealed that enlarged sylvian fissures and basal cisterns and some focally dilated sulci are compatible with a favorable response to shunt insertion in patients with NPH. The role of sylvian fissures as reservoirs of cerebrospinal fluid (CSF) analogous to those of the ventricular system has been repeatedly reported, and these patients’ condition has even been incorrectly diagnosed as
Pick disease. Reduction of sylvian fissure and cortical sulci size after shunt insertion has been repeatedly observed by several groups. Frequent findings in these patients are a moderate increase in ventricular size and evident white matter abnormalities visible on imaging studies. The finding of a significant increase in sylvian fissure size and obliteration of cortical sulci is possible but infrequent.

We believe that the findings to which Dr. Vassilouthis refers in his letter correspond to a different and infrequently encountered group of patients: those with widened sylvian fissures and obliterated cortical sulci, suggestive of an absorptive mechanism and a transmural gradient between the pressure in the ventricles and the subarachnoid space. In our opinion, sylvian fissure enlargement may result from a combination of several phenomena such as an alteration in the viscoelastic properties of the brain parenchyma, which reduces the capacity of the ventricular system to dilate, and the presence of abnormal resistance of CSF outflow. The diagnosis of these conditions is usually difficult, because patients harboring them are frequently unresponsive to the tap test and CSF dynamics studies are sometimes inconclusive. For these complex conditions, the most accurate diagnostic test is continuous monitoring of ICP.

Finally, Dr. Vassilouthis’ comments serve to emphasize the main point of our study, namely, that the criteria commonly used by some neurologists, neuroradiologists, and neurosurgeons are insufficiently specific and have predictive negative values that are too low to rule out a diagnosis of NPH and the possibility that surgery might be necessary for patients with cortical atrophy or enlarged sylvian fissures. The rare finding of sylvian fissure enlargement together with cortical sulci obliteration is an important but infrequent phenomenon that merits further investigation. These patients are usually identified by neurosurgeons and are not confused with patients who have cortical atrophy. Hence, surgery is not denied to them. However, the most frequent diagnosis in the type of patient reported in our study is that of cerebral atrophy. These patients could indeed benefit from surgical treatment, which could significantly improve their quality of life.

Maria A. Poca, M.D., Ph.D.
Juan Sahuquillo, M.D., Ph.D.
Vall d’Hebron University Hospital
Autonomous University of Barcelona
Barcelona, Spain

References


To the Editor: We read with great interest the article by Poca and colleagues (Poca MA, Mataró M, Matarín M, Arikan F, Junqué C, Sahuquillo J: Good outcome in patients with normal-pressure hydrocephalus and factors indicating poor prognosis. J Neurosurg 103:455–463, September, 2005).

We agree with the authors that the clinical conditions of patients with NPH who present with traditionally accepted markers of poor prognosis can improve after surgery, especially if the gait troubles precede the dementia onset.

On the basis of our surgical experience with more than 100 cases of hydrocephalus in adults, we think that the use of the low-pressure shunt is not advisable in patients with NPH, because subdural hematomas (SDHs) are frequent complications caused by hyperdrainage. In fact, the authors report early or late postsurgical subdural effusions in two of the 12 patients in whom shunts were inserted. One subacute SDH evacuation was performed without sequelae and one additional patient had an asymptomatic subdural collection during the months after shunt placement.

It is possible that in patients who have low-pressure shunts even very small head traumas are sufficient to produce SDHs for years after the operation. In fact, the percentage of surgical complications reported by the authors is approximately 16.6% in the first months, which in our opinion seems too high.

We believe that it is advisable to change the low-pressure value to a high-pressure one to avoid new shunt malfunctions. In our experience, we observed gait and sphincter control improvement after high-pressure shunt placement. In some cases, it is sufficient to use a medium-pressure valve along with an antisiphon device. Moreover, in recent years we have used flow-regulated lumboperitoneal shunts with good results and with no occurrences of SDH.

F. Contratti, M.D.
M. F. Friaoli, M.D.
G. Cacciotti, M.D.
University of Rome (Roma2) Tor Vergata
Rome, Italy
Neurosurgical forum

References

Response: We thank Dr. Contratti and colleagues for their letter. It provides us with the opportunity to broaden the discussion of another controversial topic in the management of patients with NPH: the choice of the most appropriate shunt for these patients to ensure maximal clinical benefit along with minimal shunt-related complications. The clinical outcomes of patients treated with NPH reported in the literature vary widely and depend on several factors: the type of hydrocephalus (idiopathic compared with secondary), the degree of clinical deterioration before shunt placement, symptom duration, comorbidity, the tests used to establish the diagnosis of NPH (all of which are associated with a variable percentage of false negatives), and the type of shunt selected. Valve selection is an essential factor in explaining outcome in these patients and, in our opinion, this topic has been insufficiently discussed in the literature. Furthermore, most studies on the outcome in patients with NPH who receive shunts describe neither the type of shunt used nor the opening pressure of the valve.

We disagree with Dr. Contratti and colleagues’ statement that the use of low-pressure shunts in patients with NPH is not advisable. Although Bergsneider, et al., emphasize that there is insufficient evidence to recommend a specific valve pressure setting for patients with idiopathic NPH, there are several points that need further discussion. Although, as pointed out by Bergsneider, et al., the studies by McQuarrie, et al., and Boon, et al., show some methodological limitations, their results support the use of low-pressure valves in these patients. Moreover, authors of other studies have reported that reducing the opening pressure of adjustable valves because of underdrainage led to subsequent clinical improvement for a considerable percentage of patients. In our department we continuously monitor ICP in all patients with suspected NPH. Our experience of more than 300 patients with this syndrome allows us to confirm that, although some patients have transitory or continuously high ICP (as did the patient shown in Fig. 2 of our article), mean ICP in idiopathic NPH is usually low and in some patients may even be negative. In these patients, medium- or high-pressure valves will function erratically. When the opening pressure of the valve is higher than the patient’s mean ICP, the valve is open only during Valsalva maneuvers, when the patient is upright (siphoning effect), and possibly during rapid eye movement sleep.

Another important point is that the use of medium- or high-pressure valves does not exclude the possibility of SDH or subdural effusion (hygroma). In their study, Boon, et al., reported a 34% incidence of subdural effusion in a group of patients with medium-pressure valves. The use of adjustable valves can reduce but not exclude nonphysiological flow rates while the patient is upright, and limit the possibility of complications related to hyperdrainage.1 In the last few years, various devices have been developed to reduce the rate of CSF drainage while patients are in upright positions. Gravitational devices and antisiphon mechanisms (the latter are based on a subcutaneous membrane that responds to negative pressure inside the shunt) have been used as separate devices added in series to the distal catheter or incorporated into the valve. These new shunts seem to reduce the incidence of underdrainage problems associated with postural change. Although an antisiphon or a gravity-compensating device used in medium- or high-pressure shunts reduces CSF drainage when the patient is upright, their use may increase the possibility of underdrainage, especially if the patient is obese. In such patients, intraabdominal pressure is usually higher than 0 mm Hg.

Other potential problems are associated with the use of antisiphon and gravity-compensating devices. Malfunctions can occur when gravitational devices become displaced from a vertical position after implantation, and CSF drainage can be hampered when the subcutaneous pressure increases over the membrane of an antisiphon device.1 In patients with complex NPH, an additional benefit of continuous ICP monitoring a few days after shunt insertion is that it allows shunt function to be studied in vivo. Our results of continuous ICP monitoring in patients who experience clinical worsening after a transient improvement allow us to suggest that caution should be exercised when using an antisiphon device in patients with idiopathic NPH, even when this device is associated with a low-pressure valve. Progressive subcutaneous scarring over the membrane of the antisiphon can produce functional underdrainage of the shunt, which may cause B waves or marked ICP irregularities to appear in some patients when sitting or standing (Fig. 1). This process can induce occult shunt dysfunction, inhibit improvement, and cause clinical worsening. We believe that in patients with idiopathic NPH, low-pressure valves should be combined with gravitational devices that are not sensitive to scarring or to external pressures.

Dual-stage, differential-pressure valve designs, such as the Miethke dual-switch valve (Aesculap AG & Co KG, Tuttlingen, Germany), which uses a double valve with different opening pressures according to whether the patient is supine (low-pressure valve) or upright (very-high-pressure valve), may be a good alternative in patients with NPH. A double valve with different opening pressures according to whether the patient is supine (low-pressure valve) or upright (very-high-pressure valve), may be a good alternative in patients with NPH. A double valve with different opening pressures according to whether the patient is supine (low-pressure valve) or upright (very-high-pressure valve), may be a good alternative in patients with NPH. At present, we use this valve in a large proportion of our patients with NPH. In our opinion, however, an opening pressure of 50 mm H2O (3.7 mm Hg) when the patient is supine is still too high for some patients in whom ICP monitoring shows very low pressures or even pressures of approximately 0 mm Hg. In two patients whose condition did not improve after shunt insertion, ICP monitoring revealed B waves. Consequently, we had to change a valve that had been functioning normally to a device with a lower opening pressure. Both patients improved after the reintervention.

The patients suffering from idiopathic NPH and cortical atrophy described in our study constitute the most fragile subgroup of patients in whom NPH is treatable. For this
We usually select an initial opening pressure. Aschoff has stated (personal communication, 2003), the problems of overdrainage are related to gravity and therefore have to be prevented by gravitational devices, not by upgrading the opening pressure of the valve. The belief that such upgrading avoids overdrainage is not entirely correct, because the opening pressure of a valve controls flow only when the patient is recumbent.

We have no interests in the companies that manufacture and distribute any of the valves or devices mentioned.

Abstract

An unusual case of an intraneural ganglion cyst of the hypoglossal nerve is presented. Only one case of this rare clinical entity has been reported previously. A 51-year-old woman presented with a 6-month history of left-sided hypoglossal nerve palsy. Magnetic reso-
We believe that these rare intraneural ganglia and cited by Baldauf, et al. The detailed examination confirmed that the lesion was an intraneural ganglion cyst. The occurrence of an intraneural ganglion cyst at the hypoglossal nerve is very rare. This case exemplifies an atypical location of a synovial cyst with cranial nerve involvement.

Intellectually, the existence of an intraneural ganglion at a new location is exciting to us, the notion of its developing in a motor cranial nerve intriguing, and the possibility of an unusual joint-related connection appealing. We agree with the famed scientist and astronomer Carl Sagan, who said, “Extraordinary claims require extraordinary evidence.” On careful scrutiny of the case, we feel that the supportive data are potentially subject to another interpretation.

We have spent the last few years putting forth a unified articular theory to explain the controversial pathogenesis of intraneural and extraneural ganglia occurring in common and uncommon locations as originating from neighboring synovial joints.1-3 We believe that these rare intraneural ganglia are related to joints through connections from (sensory) articular branches. Joint fluid extravasates through a capsular rent and extends within the epineurium along an articular branch and into a larger parent nerve. In contrast, more common joint-related extraneural ganglia result when the fluid egresses into the soft tissues. When these cysts form near nerves, they can compress them extrinsically. At times distinguishing between intraneural and extraneural ganglia is difficult. Differentiating an extraneural from an intraneural cyst is not always done (as the reader will see later) and quite frankly, such a distinction may not be easy to make at surgery due to adherence of the cyst to the nerve.4 To complicate matters further and to add to the confusion, these intra- and extraneural cysts may on occasion coexist.4

If Baldauf, et al., are correct, their case of a hypoglossal intraneural ganglion is an extraordinary one. Reviewing this case as it has been presented, however, we can confirm only cyst-related nerve compression in the region of the hypoglossal canal. We cannot reliably or definitely determine if the cyst is intra- or extraneural (an important distinction) or verify its joint connection. The preoperative magnetic resonance (MR) image that is provided (Fig. 1) demonstrates a nonspecific cyst lacking the suggestive features of an intraneural cyst. No direct imaging or operative evidence is offered to show that this cyst arises from the atlantooccipital joint; rather it is assumed to originate from this joint because of its proximity. The intraoperative photographs obtained through the endoscope do not demonstrate the stereotypical, more tubular-appearing intraneural cysts seen at other locations. In fact, a globular-appearing cyst that is more characteristic of an extraneural ganglion cyst is visualized. This cyst appears distinct and completely separate from the main hypoglossal nerve (unlabeled in Fig. 2), which apparently is not directly involved by the cystic process. The source and nature of the affected nerve branch (described as the lower branch of the hypoglossal nerve) are unclear in the photograph. Dissection of the cyst was done “under endoscopic control without the aid of the microscope.” The intraoperative nerve stimulation studies are nonspecific. The histological characteristics shown in Fig. 3 if the authors stated “confirmed an intraneural cyst” demonstrate generic myxoid connective tissue only and no associated nerve. Even the histological finding of nerve in proximity to cyst or nerve being displaced or surrounded by myxoid material is not enough to confirm a diagnosis of an intraneural ganglion; at a minimum, the cyst must lie within epineurium.

If this case does represent an intraneural ganglion cyst, we also need to explain its occurrence. Baldauf and colleagues believe that the “origin of the ganglion was the synovium of the atlantooccipital joint space.” As proponents of the articular theory,5 we must be able to link the cyst to the joint anatomically. Whereas these authors supplied us with useful information regarding the innervation of the atlantooccipital joint (through the ventral ramus of the first cervical nerve), the motor nature of the hypoglossal nerve, and its proximity to this joint, they did not provide us with the requisite connection of the joint with a potential sensory pathway. On the basis of their information, a conceivable link would be the ansa cervicalis, which could serve as a vehicle for cyst propagation, because its C-1 contribution merges with the hypoglossal nerve near the site of the cyst. If this explanation, which invokes the articular theory, were true, we would expect to have evidence of cystic involvement extending from the parent hypoglossal nerve at the level of the atlantooccipital joint into the rootlets of the hypoglossal nerve near the brainstem (assuming this was the path of least resistance). We cautiously offer this explanation; we do not know if this is anatomically or clinically plausible. Without a verifiable articular branch connection or involvement of the parent hypoglossal nerve, however, we reluctantly would have to invoke the notion of de novo formation of this cyst isolated to a short nerve branch in this particular instance (that is, supporting the degenerative theory—the other major theory to explain intraneural ganglia). An alternative explanation is that the ganglion cyst reported by Baldauf, et al., is an extraneural one that compressed the hypoglossal nerve extrinsically and probably arose from a degenerative atlantooccipital joint. In fact, the authors state that the “hypoglossal nerve branch is surrounded by the cyst.” We believe that this example would then be directly analogous to the case reported by Mujic and colleagues1 and cited by Baldauf, et al. The detailed operative findings and images in the paper by Mujic, et al., documented an extraneural cyst. The bilobular cystic tumor was described as “compressing and displacing the medial branches of the XII nerve.”6 In addition, no associated neural tissue was identified histologically. Baldauf, et al., stated that the case of Mujic and colleagues was the “only case of this rare clinical entity to have been reported previously,” interpreting this “compressive cyst”7 (an extraneural ganglion) as one that “infiltrated the nerve” (an intraneural ganglion).

In the end, we are left with many questions. Is a hypoglossal intraneural ganglion possible, and if so, can it be joint related? Can the atlantooccipital joint give rise to an intraneural as it does to an extraneural ganglion? Can the first cervical nerve have an articular branch, even when this nerve in some cases lacks a dorsal root through so-called “wrong way ventral afferents?”

Proving a theory related to a rare entity and based largely on retrospective reports has obvious challenges and lim-
iterations. Previously, we have shown that radiologists and surgeons who claimed that articular branch connections did not exist (thereby refuting the articular theory) simply did not recognize them.\textsuperscript{3–5} The words of English poet William Cowper resonate: “absence of proof is not proof of absence.” As we suggest in this letter, we must also be cautious when interpreting supposed cases of intraneural ganglia (with or without joint connections) and be absolutely, positively certain that they are indeed intraneural ganglia.

To prove or disprove our unifying theory for intraneural ganglion cysts, we must collaborate and strive to provide the strongest scientific evidence possible so that others can interpret and reinterpret the supportive data critically for themselves if they are to embrace the authors’ conclusions wholly. We should establish protocols on how to best evaluate these curiosities and to answer these types of questions.\textsuperscript{2} We must review these findings lest they be misinterpreted. This standardized methodology will allow others to analyze the potential joint connection, the normal or pathological nature of the articular branch, and the specific relationship of the cyst to the nerve. Ultimately, this structured, organized approach will improve patient outcomes (for example, by decreasing recurrences if articular connections are not identified)\textsuperscript{9} and will definitively put to rest the century-old controversy related to the pathogenesis of intraneural ganglion cysts. The common denominator in this process is extraordinary evidence. Authors need to provide it, reviewers must demand it, and readers should come to expect it.

ROBERT J. SPINNER, M.D.
STEPHEN W. CARMICHAEL, PH.D.
JOHN L. D. ATKINSON, M.D.
Mayo Clinic
Rochester, Minnesota

References


RESPONSE: We thank Dr. Spinner and colleagues for their thoughtful comments regarding our paper. Of course, we know their theory about the importance of the articular (sensory) branch as cited in our paper;\textsuperscript{1} however, the location of a ganglion cyst in relation to the hypoglossal nerve is still unusual. In our paper, we discussed different theories to explain pathological conditions that might have led to the cyst development in our case.

The intraoperative view and intraoperative nerve stimulation demonstrated that only the lower branch of the hypoglossal nerve was affected by the cyst. We had the impression that this part of the nerve was infiltrated and expanded by the cyst, as is known to occur because of intraneural cysts. The hypoglossal nerve cyst looked the same as intraneural ganglion cysts of the peroneal nerve, of which we had four cases.

To verify the histopathological evidence of an intraneur al cyst, immunohistological staining for S-100 protein was performed (Fig. 1). The finding of positively stained (that is, hypoglossal) nerve fibers infiltrated and surrounded by myxoid connective tissue is obvious.

In conclusion, we still believe that the case presented is intraneural in origin. Because of the limited approach and partial exposure of the cyst, however, the possibility that the cyst was extraneural cannot be excluded definitely.

JORG BALDAUF, M.D.
SILKE VOGELGESANG, M.D.
HENRY W. S. SCHROEDER, M.D.
Ernst-Moritz-Arndt University
Greifswald, Germany

Pressure Gradients in Experimental Hydrocephalus Model

TO THE EDITOR: We read with great interest the article by Penn and colleagues (Penn RD, Limninger AA, Miesel K, Lu SN, Stylos L: Pressure gradients in the brain in an
Neurosurgical forum


Abstract

Object. The goal of this investigation was to establish whether pressure gradients exist between the ventricles, brain tissue, and subarachnoid space when acute or chronic hydrocephalus develops. Such gradients are hypothesized by many models of hydrocephalus, but considerable controversy continues about their existence.

Methods. A stereotactic frame was used for surgery in dogs to implant pressure sensors within the right lateral ventricle, the frontal lobe, and forward in the subarachnoid space. The dogs were allowed to recover for 10 to 14 days postoperatively. Then, 800 mg of sterile kaolin in water was injected into the cisterna magna region by using a percutaneous approach. Both real-time and long-term intracranial pressures were measured.

Of the six dogs, one experienced an intracranial hemorrhage, one dog displayed status epilepticus after a second injection of kaolin and was killed, one experienced acute hydrocephalus, and three experienced mild chronic hydrocephalus. No consistent pressure differences were found in any dog between the ventricle, brain, and subarachnoid space before kaolin administration or afterward when hydrocephalus developed. In addition, no pulse pressure gradients occurred between the brain and the ventricle or subarachnoid space.

Conclusions. Precise monitoring of pressure before and during the development of hydrocephalus did not detect pressure gradients between the ventricle, brain, and subarachnoid space. This was true for long-term measurements over weeks and for real-time measurements that allowed accurate assessment of pulse pressures. Theories predicting pressure gradients greater than the resolution of these sensors (0.5 mm Hg) across brain tissue have to be reevaluated in light of these findings.

The authors used the well-established kaolin model of hydrocephalus in conjunction with a novel method of intracranial pressure (ICP) monitoring performed using telemetry with the Insite Monitoring System (Medtronic Neurological, Minneapolis, MN). Six animals implanted with pressure sensors experienced hydrocephalus in a predictable fashion. However, the authors found no evidence for pressure gradients in the brain, either in the setting of acute or chronic hydrocephalus. Importantly, they also found no evidence of differences in pulse pressure waveforms between the compartments studied.

We applaud their study and concur with their findings. Previously, we showed the absence of a detectable pressure gradient in the brain in response to acute increases in ICP. In our model, bilateral ventricular catheters were placed and a Camino pressure transducer (Camino Laboratories, San Diego, CA) was implanted in the cortical subarachnoid space. Measurements incorporated perturbations in ICP after the acute inflation of a subdural balloon. The immediate responses to balloon inflation were identical in all three compartments, regardless of whether recordings were obtained from the ipsilateral ventricular space (that is, on the same side as the subdural balloon inflation), the contralateral ventricular space, or the contralateral cortical subarachnoid space.

The ventricular response to changes in ICP (for example, enlargement as seen in hydrocephalus or compression in pseudotumor cerebri) is therefore not a function of transcranial pressure gradients. Rather, it is a function of the intrinsic viscoelastic properties or compliance of the brain itself. We have labeled this term Kb in our model of the response to ventricular volume to derangements in cerebrospinal fluid outflow resistance. Clinically, we have found that the ventricular response to intervention directed at influencing Kb is predictable (for example, in the setting of ventriculomegaly in the presence of ventriculoperitoneal shunts) and increases resistance for absorption of cerebrospinal fluid in the cortical subarachnoid space. Mild jugular compression increases venous outflow resistance and hence brain turgor. Jugular compression is instituted by placement of an ace bandage circumferentially around the neck at a two-finger tightness. In this setting, the bandage tends to reduce ventricular dilatation (Fig. 1).

![Fig. 1. A and B: Axial computerized tomography (CT) scans. C: photograph of the patient. This 24-year-old woman with a history of hydrocephalus and multiple shunt revisions after resection of a hemangioblastoma when she was 7 years of age presented with acute shunt failure. The patient underwent revision of her shunt; however, she subsequently complained of severe headache. The CT scans obtained after the revision demonstrated slit ventricles, and a diagnosis of over-shunting was established. The patient’s shunt was therefore revised to one containing an antisiphon device, after which her ventricles enlarged (A). We hypothesized that the patient’s ventricular sensitivity to the presence of the antisiphon device was due to insufficient brain turgor, and a cervical venous tourniquet was applied to two-finger tightness. The patient’s ventricles responded dramatically to this intervention (B), and her symptoms resolved. The patient recovered and was discharged home, where she continues to apply the tourniquet nightly (C).](image-url)
Finally, despite the absence of experimental evidence for the existence of transcranial pressure gradients, especially in the setting of communicating hydrocephalus, the authors propose that microgradients (pressure gradients $\leq 0.5$ mm Hg, the experimental limitations of their study) are sufficient to account for changes in ventricular volume. We agree that this area merits further study, and we would be interested in further investigations on the topic should the existence of such microgradients be demonstrated conclusively.

GREGORY LEKOVIC, M.D., PH.D., J.D.
HAROLD L. REKATE, M.D.
Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center
Phoenix, Arizona

References

RESPONSE: We appreciate Lekovic’s and Rekate’s comments on our paper. Together their experiments and ours demonstrate that the pressure differences between the ventricles and the subarachnoid space are small. This holds true for healthy patients as well as for those harboring hydrocephalus and mass lesions, as long as the cerebrospinal fluid (CSF) pathways are open. Although the pressure differences between the ventricles and subarachnoid space in humans cannot be measured directly due to the small magnitude, our cine magnetic resonance imaging CSF flow velocity measurements in healthy volunteers and hydrocephalic patients can accurately quantify the CSF flow during the cardiac cycle. From these measurements, obtained using fluid dynamics principles together with advanced three-dimensional reconstruction algorithms of brain geometry, we have accurately predicted pressure differences and found these to be below 50 pascals (133 pascals = 1 mm Hg) in patients with hydrocephalus and below 10 pascals in healthy volunteers. Without these small pressure differences, CSF flow could not occur. We also found that the amplitude of the ICP wave during the cardiac cycle is much larger in hydrocephalic patients than in healthy volunteers. In fact in hydrocephalic patients the pulsatile CSF flow is increased by a factor of five. It is still unclear how these small pressure gradients relate to the massive changes in ventricular size observed in hydrocephalic patients. Lekovic and Rekate drew attention to both the viscoelastic properties of the porous brain tissue and how it could affect brain size, and illustrate their points with a clinical example. It is the goal of our work to quantify these changes to provide an accurate physical description of what takes place in brain tissue when hydrocephalus is present and to provide an understanding of what forces are involved in creating it. If we understand these forces, we can look forward to protecting the brain when hydrocephalus occurs and to devising new treatments.

RICHARD D. PENN, M.D.
The University of Chicago Medical Center
ANDREAS A. LINNINGER, PH.D.
The University of Illinois of Chicago
KEITH MIESEL, B.S.
STEVEN NING LU, M.S.
LEE STYLOS, PH.D.
Medtronic, Inc.
Minneapolis, Minnesota

Hypervolemia in Cerebral Vasospasm


Abstract
Object. Arterial vasospasm is the most common cause of delayed ischemic neurological deficits (DINDs) and one of the major causes of disability following subarachnoid hemorrhage (SAH). Current management of vasospasm involves intravascular volume expansion and hemodynamic augmentation with the goal of increasing cerebral blood flow (CBF). The purpose of this study was to examine the effects of volume expansion on regional (r)CBF in patients with DIND following SAH.

Methods. The authors measured quantitative rCBF on positron emission tomography (PET) scans in six patients with aneurysmal SAH who had developed clinical signs of vasospasm. All patients were kept in a euvolemic state prior to the onset of vasospasm. At the onset of vasospasm, global and rCBF were measured before and after the administration of a normal saline bolus of 15 ml/kg administered over 1 hour. Two patients then received saline infusions of 5 ml/kg × hr over the following 2 to 3 hours and underwent hourly serial CBF measurements. Global and rCBF data were calculated in each patient. The mean rCBF in areas with low flow at baseline (≤ 25 ml/[100 g × min]) increased from 19.1 ± 3.0 to 29.9 ± 9.7 ml/[100 g × min] (p = 0.02) with volume expansion. This change was sustained over the following 2 to 3 hours. Pulmonary capillary wedge pressure, mean arterial blood pressure, cardiac output, and central venous pressure did not change significantly during this intervention.

Conclusions. In euvolemic patients with vasospasm, intravascular volume expansion with a normal saline bolus raised CBF in regions of the brain most vulnerable to ischemia.

We agree with the authors that the role of hypervolemia alone is uncertain in the treatment of clinically significant vasospasm. Therefore, they have to be congratulated on investigating the effect of volume expansion on rCBF in patients in a euvolemic state who have DIND.

Their results demonstrated that a 15 ml/kg saline bolus significantly increased rCBF in areas with low CBF (≤ 25 ml/[100 g × minute]), but had no influence on bihemispheric CBF, rCBF in areas without vasospasm, rCBF with high baseline rCBF, and rCBF in areas with vasospasm with high baseline CBF. They repeatedly state that these increases in rCBF occurred without a concomitant significant rise in systemic hemodynamic parameters. Accordingly, this is supported by the conclusion of the paper, the reader will
take this study as evidence that patients with DIND will benefit from the use of hypervolemia.

On this point we disagree. Comparing the numbers for the change in the hemodynamic parameters following the volume expansion as given in their Table 2, there was an increase in mean arterial blood pressure (MABP) from 110.2 mm Hg before to 123.7 mm Hg after saline infusion. We are not sure why the authors have ignored this increase in MABP as one cause for the change in rCBF. Instead, they stated that “the physiological mechanism for these changes remains unclear.” It may be that the probability value of their statistical test did not reach significance when comparing MABP before and after saline infusion; however, these tests are highly influenced by the sample size (six patients).

If we believe our clinical or experimental findings, we assume that they are reproducible in a larger cohort of patients. If they are reproducible, we should not be forced to change our interpretation of the data.

We would consider a mean increase in MABP by 12% to be hemodynamically relevant, albeit statistically not significant, in a cohort of six patients. In light of this finding, there is no evidence that volume expansion alone without a concomitant increase in MABP is a beneficial measure for patients with DIND. In fact in our own experience we have found that the hypervolemic component of triple-H treatment (with the other components being induced hypertension and hemodilution therapy) was less effective and associated with a higher complication rate. Moreover, in this study only the short-term effect of volume expansion in patients previously in a euvolemic state was investigated, and measurements were obtained at a maximum of 4 hours. The effect of continuing hypervolemia in patients for several days remains unclear.

It can be argued that increasing blood pressure is part of the treatment goal when using hypervolemia alone. This notion confounds the nomenclature, however, and an elevation in blood pressure can be achieved more effectively and with fewer complications with the use of high-normal normovolemia and vasopressor agents.

ANDREAS RAABE, M.D.
University of Frankfurt am Main, Germany
BERTIL ROMNER, M.D.
University Hospital of Lund, Sweden

References

RESPONSE: We thank Drs. Raabe and Romner for their interest in our recent paper, but are surprised that they disagree with our conclusion that a fluid bolus can improve CBF in low-flow regions in patients with symptomatic vasospasm. The basis for their disagreement is that our study demonstrated a numerical but not statistically significant increase in blood pressure, which they believe is solely responsible for the rise in CBF we observed in our patients. Additionally, they point to their experience in treating vasospasm, in which hypervolemia was less effective than hypertension in improving the oxygen tension of brain tissue and was associated with more complications.

We believe our conclusions are valid and support our current use of intravascular volume expansion in treating vasospasm. The purpose of our study was to determine if a fluid bolus would increase CBF in patients who were in a euvolemic state and had symptomatic vasospasm. It was not our intention to determine the physiological basis for changes in CBF, but rather to assess the response to a clinical intervention. We clearly state in the concluding paragraphs of our paper that volume expansion may not be appropriate in all patients, and we limit our recommendations to the use of a fluid bolus as a temporizing measure in preparation for pharmacological hemodynamic augmentation or endovascular therapy. We did not study the sustained use of hypervolemia or draw any conclusions regarding it.

In addition, there were no significant correlations between change in CBF and any hemodynamic parameter. Although we accept the criticism that some of the hemodynamic changes would likely have been significant if a large number of patients had been studied, it is important to point out that both blood pressure and cardiac index rose to a similar degree. Thus, to argue that the response was due to an increase in blood pressure alone is not valid.

Finally, our unpublished observations suggest that pharmacological elevation of blood pressure with phenylephrine produces a much more robust increase in CBF than we saw with volume expansion. If this observation is borne out, we would then draw conclusions similar to those of Raabe and Romner. The present report simply highlights the finding that, even in patients in a euvolemic state, a fluid bolus can effectively improve CBF in low-flow regions while preparations for more sustained treatment are undertaken.

MICHAEL N. DIRINGER, M.D.
Washington University School of Medicine
St. Louis, Missouri