Early deterioration of cerebrospinal fluid dynamics in a neonatal piglet model of intraventricular hemorrhage and posthemorrhagic ventricular dilation

Laboratory investigation

KRISTIAN AQUILINA, F.R.C.S. (NEUROSURG), 1–3 ELA CHAKKARAPANI, M.R.C.P.C.H., 1,2 AND MARIANNE THORESEN, PH.D. 1,2,4

1University of Bristol School of Clinical Sciences; 2Neonatal Neuroscience, St. Michael’s Hospital; 3Department of Neurosurgery, Frenchay Hospital, Bristol, United Kingdom; and 4Institute of Basic Medical Sciences, University of Oslo, Norway

Object. The optimal management of neonatal intraventricular hemorrhage (IVH) and posthemorrhagic ventricular dilation is challenging. The importance of early treatment has been demonstrated in a recent randomized study, involving early ventricular irrigation and drainage, which showed significant cognitive improvement at 2 years. The objective of this study was to define the changes in CSF absorption capacity over time in a neonatal piglet model of IVH.

Methods. Ten piglets (postnatal age 9–22 hours) underwent intraventricular injection of homologous blood. A ventricular access device was inserted 7–10 days later. Ventricular dilation was measured by ultrasonography. Serial constant flow infusion studies were performed through the access device from Week 2 to Week 8.

Results. Seven piglets survived long term, 43–60 days, and developed ventricular dilation; this reached a maximum by Week 6. There was no significant difference in baseline intracranial pressure throughout this period. The resistance to CSF outflow, $R_{\text{out}}$, increased from 63.5 mm Hg/ml/min in Week 2 to 118 mm Hg/ml/min in Week 4. Although $R_{\text{out}}$ decreased after Week 5, the ventriculomegaly persisted.

Conclusions. In this neonatal piglet model, reduction in CSF absorptive capacity occurs early after IVH and accompanies progressive and irreversible ventriculomegaly. This suggests that early treatment of premature neonates with IVH is desirable.

(http://thejns.org/doi/abs/10.3171/2012.8.PEDS11386)

Key Words • cerebrospinal fluid dynamics • hydrocephalus • neonatal intraventricular hemorrhage • neonatal piglet model • posthemorrhagic ventricular dilation • resistance to cerebrospinal fluid outflow

Intraventricular hemorrhage and PHVD remain important problems in neonatal care. Multiple interventions, including serial lumbar punctures, administration of acetazolamide, insertion of a ventricular access device for regular aspiration of CSF, as well as combined drainage, irrigation and fibrinolytic therapy (DRIFT) have not reduced the need for permanent CSF diversion.51,52,56,58 Development of chronic hydrocephalus is related to progressive fibrosis in the basal cisterns, with reduction in the absorptive capacity of CSF.38 Cytokines with fibrinogenic potential, such as TGF-β and VEGF, are known to be involved in the development of hydrocephalus after neonatal IVH,7,54 as well as after SAH in adults.15,24 Progression from IVH to PHVD is readily monitored by serial ultrasonography at the bedside. However the time course of the underlying reduction in CSF absorptive capacity is unclear, and the optimal timing of interventions remains controversial. Early and aggressive irrigation and fibrinolysis, as in DRIFT, has been associated with significant cognitive benefit at 2 years.57 A trial comparing

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
early against late aspiration of ventricular CSF (ELVIS) is underway (www.bris.ac.uk/clinicalsciencenorth/neonatal/ri/phitt.html). Several studies have used animal models of hydrocephalus to study changes in CSF dynamics related to progressive ventricular enlargement.4,8,21,26,30,40,41 Most of these animal models were based on injection of kaolin into the cisterna magna at varying ages. The pathophysiology of kaolin-induced hydrocephalus is fundamentally different from that of the posthemorrhagic type. In this study, we used our neonatal piglet model of IVH and PHVD to evaluate serial changes in CSF dynamics throughout the chronic phase of PHVD development.1

Methods

This study was conducted under a project license for animal testing from the United Kingdom Home Office.

Intraventricular Hemorrhage

Ten crossbred Landrace piglets, postnatal age 9–22 hours (median 22) and weight 1.2–2.2 kg (median 1.9) underwent intraventricular injection of homologous blood as previously described.1 In this model, brains extracted at 3 days show clotted blood in the subarachnoid space and basal cisterns. Theperfused brain at 6–8 weeks demonstrates significant ventriculomegaly (Fig. 1). Briefly, following induction of general anesthesia (0.8% halothane and 60%-70% N2O), animals underwent endotracheal intubation and were ventilated to an end-tidal CO2 of 4.5–5.5 kPa. Umbilical arterial and venous catheters were inserted, allowing continuous invasive arterial blood pressure monitoring. Blood glucose was maintained at 3–10 mmol/l and rectal temperature at 38°C–39°C, the normal body temperature for piglets. Antibiotic prophylaxis (gentamicin 2.5 mg/kg and cephalothin 20 mg/kg) was administered intravenously twice daily until all vascular lines were removed. Two-channel parietal amplitude-integrated encephalograms (BrainZ Ltd) were recorded continuously throughout the baseline, injection, and recovery phases.

A surgical anterior fontanel, 1.5 cm in diameter, was fashioned anterior to the coronal suture. An intraparenchymal ICP monitor (Codman MicroSensor ICP transducer, Codman/Johnson and Johnson Professional Inc.) was inserted through a separate craniotomy. To replicate the elevated hematocrit in neonates, and in accordance with our earlier study in which blood with elevated hematocrit resulted in more pronounced ventricular dilation, homologous blood, obtained from the umbilical artery line and mixed with buffered sodium citrate, was centrifuged at 6000 rpm for 10 minutes; four-fifths of the plasma was then removed and the red cells were resuspended in the residual plasma anduffy layer. This blood, with an elevated hematocrit, was then used for intraventricular injection. Under ultrasound guidance through the fontanel, a 25-gauge cannula was inserted into the brain parenchyma through a craniotomy 8 mm lateral to the midline and 5 mm posterior to bregma; 4.0 ml of blood was injected at 2.0 ml/hour using a Harvard syringe driver. Intermittently, during the second half of the injection, an ultrasound probe on the fontanel confirmed the presence of intraventricular blood.

On completion of intraventricular injection, the cannula and ICP monitor were removed. Anesthesia was discontinued, and the piglets were extubated on the return of spontaneous ventilation. Animals progressed from intravenous fluids to bottle-feed (Faramate, Volac Feeds) over 24 hours. A neurological scoring system, initially devised for a piglet model of posthypoxic encephalopathy, was used to characterize any neurological deficit in the first 24 hours.50 The piglets were then nursed in an appropriate warm animal pen. All vascular lines were removed by 3–5 days.

Measurement of Ventricular Size

Animals underwent weekly brain ultrasonography through the artificial fontanel. Anesthesia was not necessary for this procedure. A satisfactory view of the ventricular system was obtained on most occasions. Serial measurements of the thalamooccipital distance, measured from the apex of the occipital horn to the pulvinar of the thalamus and the maximum unilateral frontal horn width, measured from the septum pellucidum to the most lateral point on the wall of the frontal horn, were obtained as has been described in clinical practice.12

Implantation of Ventricular Access Devices

Within 7–10 days of IVH, 6 animals had developed sufficient ventriculomegaly to allow insertion of a ventricular access device. Animals were anesthetized, intubated, and ventilated as above. A peripheral venous cannula allowed administration of intravenous fluids and prophylactic antibiotics peroperatively. The piglet’s head was partially shaved, cleaned thoroughly with antiseptic solutions and draped. The ultrasound probe was placed in a sterile cover and held over the fontanel to determine the

---

**Fig. 1.** A: Coronal brain section, at the level of the atrium of the ventricles, from piglet killed within 24 hours of intraventricular blood injection, showing unclotted blood within the ventricle. **B and C:** Basal (B) and sagittal (C) views of whole brain from piglet killed 3 days after injection; organized hematoma is evident within the basal cisterns. **D:** Coronal section, at the level of the temporal horns, of perfused and formaldehyde-fixed brain from piglet killed 8 weeks after injection showing severe dilation of the third and lateral ventricles.

K. Aquilina, E. Chakkarapani, and M. Thoresen

---

*J Neurosurg: Pediatrics / Volume 10 / December 2012*
ideal location for insertion of the reservoir. When possible this was placed in the widest part of the ventricle, usually the atrium (Fig. 2A). A bur hole was drilled through a curvilinear incision large enough to allow adequate skin cover over a neonatal 12-mm reservoir dome (Fig. 2B). A 2-cm ventricular catheter was attached to the reservoir. Occasionally, shorter catheters were required, depending on ventricular depth and size. The ventricle was cannulated under direct ultrasound guidance with a 25-gauge cannula. Once CSF was obtained, the ventricular catheter was passed through the same tract into the ventricle. Ultrasonography confirmed that the tip of the ventricular catheter was correctly positioned within the ventricle (Fig. 2C). The base of the reservoir was allowed to sit on the skull. Intrathecal vancomycin and gentamicin were administered through the reservoir. The skin was closed over its dome with a single layer of interrupted 4-0 nylon sutures. The wound was then dressed with dressing spray (Opsite Spray). Analgesic medication was administered intramuscularly prior to discontinuation of anesthesia. Postoperatively, piglets were kept under close observation in the laboratory until feeding was reestablished prior to return to the animal pen.

The ventricular access device incision was inspected daily throughout the survival period, and areas of suspected superficial wound breakdown were examined under anesthesia; debridement and resuturing was necessary on 2 occasions.

**Measurement of ICP**

Intracranial pressure was measured through the ventricular access device under brief isoflurane and intramuscular ketamine (10–15 mg/kg) anesthesia. Under sterile conditions, one 25-gauge butterfly needle pre-primed with normal saline was inserted into the ventricular access device. The tubing of the needle was connected to a fluid-filled transducer, in turn connected through stiff tubing to a patient monitor. The transducer was zeroed at the level of the middle of the head, representing the zero pressure point of the ventricular system. Transduction of an appropriate ICP waveform confirmed continuity of the needle, reservoir, and ventricular catheter with the intraventricular fluid. End-tidal CO₂ was maintained at 4.5–5.5 kPa. At the end of the recording period, an intrathecal dose of vancomycin and gentamicin was administered. Data were recorded to the ICM+ software at a resolution of 100 readings per second.¹⁹

**Constant Flow Ventricular Infusion Test**

Serial constant flow ventricular infusion tests, as previously described,¹⁹ were performed through the ventricular access device. After baseline ICP recording, a second 25-gauge butterfly needle was inserted into the ventricular access device (Fig. 2D). This pre-primed needle was attached to a 20-ml syringe containing normal saline. Using a Harvard syringe driver, fluid was injected at a constant rate of 0.2 ml/minute. Although the rate generally used in clinical practice is 1.5 ml/minute, 0.2 ml/minute was found to be the ideal rate to produce a steady, slow rise in ICP in this model. Infusion continued until a plateau was reached. The algorithm in the ICM+ software was used to calculate the resistance to CSF outflow (Rₑₒₙ). Steady deep anesthesia and constant end-tidal CO₂ levels were maintained throughout the infusion test.

**Long-Term Survival**

Animals were weaned at 21 days and phased over to dry chow. Iron supplementation was administered intramuscularly during the first week (Leodex 20% iron injection, Leo Pharmaceuticals; 1 ml). The piglets were weighed daily during the first 2 weeks and weekly subsequently. At termination of the study, animals were killed by perfusion-fixation through the carotid arteries with normal saline and phosphate-buffered formaldehyde under deep anesthesia. Their brains were subsequently removed and evaluated for posthemorrhagic changes and hydrocephalus.

**Statistics**

Unless otherwise specified, results are presented as median and full range or interquartile range, IQR. Graph Pad Prism 4.0 and SPSS for Windows version 14.0 were used to evaluate data. A p value < 0.05 on 2-sided testing was considered significant. ANOVA was used to compare multiple samples, using the Dunnett posttest comparison to identify differences over time; correlations were evaluated with the Spearman test.

**Results**

**Long-Term Survival**

Seven piglets survived for 43–60 days (median 51 days). Three animals died prematurely of experimental complications. One piglet died of respiratory problems at

---

**Fig. 2. A–C:** Ultrasonographic images and intraoperative photograph showing the insertion of ventricular access device. The device is inserted into the lateral ventricle (indicated by asterisk, A) under ultrasound guidance. The intraventricular component (catheter) is indicated by the arrowhead (C). **D:** Experimental setup for ventricular infusion test—two 25-gauge needles are inserted percutaneously into the reservoir, one connected to the pressure transducer and one to an infusion pump.
24 hours of age following extubation after IVH. A second piglet died at 17 days of progressive sepsis, including pneumonia and peritonitis, and the third animal died of intracranial hypertension after developing de novo intraventricular and intracerebral hemorrhage when an attempt was made to remove a ventricular access device that had become blocked. The other 7 piglets gained weight satisfactorily throughout their survival period.

Ventricular Dilation

Ventricular dilation developed in 8 or 10 animals. The median thalamooccipital distance increased from 3.6 mm (IQR 2.5–4.6 mm) in Week 1 to a maximum of 11.3 mm (IQR 7.4–11.8 mm) in Week 6. This distance tended to remain stable over the last 2 weeks (Fig. 3A).

The maximum frontal distance changes followed a similar pattern, increasing from 2.1 mm (IQR 1.1–2.5 mm) in Week 1 to a maximum of 8.4 mm (IQR 6.3–1.0 mm) in weeks 6 and 7 (Fig. 3B).

A high correlation between thalamooccipital distance and maximum frontal distance was demonstrated (Spearman r = 0.79, p < 0.0001) (Fig. 3C).

Baseline ICP

In the 6 animals with the highest degree of ventricu-

lomegaly, where a ventricular access device had been inserted, the median baseline ICP in Week 2 was 7.0 mm Hg (IQR 6.9–9.5 mm Hg). Although the median ICP rose to 10 and 9.4 mm Hg in Weeks 3 and 4, respectively, there was no significant difference in the measured baseline ICP throughout the monitoring period (Fig. 4 upper). There was also no significant difference from ICP values obtained through the intraparenchymal monitoring device prior to commencement of intraventricular blood injection at the beginning of the study (median 5 mm Hg, IQR 2–5.5 mm Hg).

Infusion Tests and $R_{\text{out}}$

A total of 26 infusion tests were performed, from Week 2 to Week 8. The median infusion test duration was 17.8 minutes (IQR 11.4–25.7 minutes). A median volume of 4.1 ml (IQR 2.6–5.3 ml) was injected. The median change in ICP from baseline to plateau was 14.1 mm Hg (IQR 11.3–18.8 mm Hg). The median $R_{\text{out}}$ increased from 63.5 mm Hg/ml/min in Week 2 to 71.3 mm Hg/ml/min in Week 3 and 118 mm Hg/ml/min in Week 4 (p = 0.02, ANOVA across all weeks; p < 0.05 for comparison between Week 2 and Week 4 and between Week 2 and Week 5, Dunnett posttest comparison). The median $R_{\text{out}}$ continued to increase to 185 mm Hg/ml/min in Week 5.

![Fig. 3. A–C: Graphs showing progressive changes in thalamooccipital (A) and maximum frontal difference (B) throughout the survival period and correlation between the 2 parameters (C). Good correlation was demonstrated between the 2 parameters in this model (Spearman r = 0.79, p < 0.0001). D and E: Method of measurement of thalamooccipital distance (D) and maximum frontal distance (E).](image-url)
there were too few observations to allow calculation of IQR.)
whiskers full range. (For some of the measurements there were too few observations to allow calculation of IQR.)

before decreasing again to 50 mm Hg/ml/min in Week 8 (Fig. 4 lower).

**Correlation Between Ventricular Dilation and Changes in CSF Dynamics and Gross Pathology**

The progressive change in $R_{\text{out}}$ was accompanied by progressive ventricular dilation (Fig. 5). However, reduction in $R_{\text{out}}$ after Week 5 was not associated with reduction in ventricular size.

Evaluation of perfused brains at the end of the survival period demonstrated ventriculomegaly as well as diffuse organized fibrous adhesions in the subarachnoid space (Fig. 6). The adhesions were more extensive and dense than those identified in brains from the 2 piglets dying earlier in this study (24 hours and 17 days post-IVH) from nonintra-cranial causes. Hematoxylin and eosin preparations of the adhesions in the basal cisterns showed extensive fibrous changes in the cisternal spaces (Fig. 7).

**Discussion**

Although the precise process by which neonatal IVH causes PHVD is unclear, progressive obliterative arachnoiditis in the basal cisterns, associated with meningeal fibrosis in the region of the fourth ventricle outlet foramina, with blockage of the arachnoid villi by particulate debris, is probably central to this progression.

The levels of TGF-$\beta$ and other cytokines are elevated shortly after IVH, and their levels in the CSF correlate with the degree of ventriculomegaly. In a rat IVH model, increased TGF-$\beta$ expression was associated with increased deposition of laminin, fibronectin, and vitronectin in the extracellular matrix. In this current study, we sought to define the progressive change in derangement of CSF absorptive capacity following IVH, and to correlate it with changes in ventricular size and ICP.

We used the constant flow ventricular infusion test to evaluate serial CSF dynamics throughout the survival period. This test, initially described by Katzman and Hussey in 1970, involves the infusion, at a constant rate, of sterile normal saline into the subarachnoid or intraventricular space. Cerebrospinal fluid pressures are monitored during infusion. The infusion rate is approximately twice the rate of CSF production; if CSF absorption is intact, a modest and gradual elevation of CSF pressure occurs. A computerized version of this test is now in use, using the ICM+ software (Cambridge, UK). The resistance to CSF outflow, $R_{\text{out}}$, is determined as the difference between the plateau pressure reached during infusion and the resting ICP, divided by the infusion rate. This test has been used to diagnose normal pressure hydrocephalus, to evaluate the need for CSF diversion in patients with ventriculomegaly, and to detect shunt malfunction; it is considered a reliable evaluation of compensatory reserve in hydrocephalus. As in IVH, progressive fibrosis in the subarachnoid space after SAH leads to impairment of CSF drainage and hydrocephalus. Several studies have evaluated CSF dynamics in SAH. Arachnoid membrane thickening was demonstrated on scanning electron microscopy in an experimental model of SAH in adult dogs. Gjerris et al. studied 33 patients with SAH, conducting both ICP monitoring and $R_{\text{out}}$ measurements. In the chronic phase, at least 7 weeks after SAH, ICP was within normal range, but $R_{\text{out}}$ was elevated. Insertion of a ventriculo-peritoneal shunt led to reduction in ventricular size, resolution of periventricular lucency, and significant clinical improvement.

Kaolin, injected microsurgically into the cisterna magna, closes the foramina of Luschka and Magendie by a meningeal inflammatory reaction. The connection between the ventricular and intracranial subarachnoid CSF compartments is therefore obstructed, leading to ventriculomegaly. Although the location of the obstruction, at the fourth ventricle outlet foramina and the subarachnoid space, is similar to that in PHVD, the pathophysiology is essentially different. In IVH the iron released from heme days after hemorrhage catalyzes lipid peroxidation and exacerbates excitotoxicity. Non–protein bound iron levels in the CSF are markedly increased for several weeks after human neonatal IVH, enhancing the formation of reactive oxygen species at a time when antioxidant enzymes are not yet fully developed. In addition, the coagulation cascade releases thrombin, known to induce apoptosis in cultured neurons and astrocytes.
Platelet granules within the intraventricular clot release TGF-β as lysis proceeds.\textsuperscript{22} TGF-β is also synthesized de novo by recruited macrophages and the choroid plexus.\textsuperscript{16} TGF-β is a potent fibroblast stimulator and leads to an increase in extracellular matrix deposition.\textsuperscript{4}

Several animal studies have analyzed CSF dynamics in models of kaolin-induced hydrocephalus. In a study on kaolin-induced acute and chronic hydrocephalus in adult cats, up to 40\% of animals developed severe spasticity within 5–7 days. Perfusion studies into the lateral ventricles at 1 and at 3 weeks showed dramatic reduction in ventricular pressure in the chronic phase, with a 6-fold increase in CSF absorption.\textsuperscript{27} This suggests an arrested form of chronic hydrocephalus, where a low-pressure

![Fig. 5. A–C: Serial changes in $R_{\text{out}}$ on ventricular infusion testing with corresponding sagittal ultrasound ventricular images on Days 12 (A), 18 (B), and 22 (C) in 1 piglet. A progressive change in $R_{\text{out}}$ was associated with, and preceded, enlargement of the ventricular system.](image)

![Fig. 6. Basal view of extracted brains from a noninjected piglet (A), a piglet killed 24 hours after intraventricular injection (B), and a piglet killed 2 weeks after injection (C). Extensive subarachnoid blood is still evident at 24 hours (B). This disappears by 2 weeks, when hemosiderin-stained fibrinous adhesions begin to appear (arrow, C).](image)
CSF dynamics in neonatal piglet intraventricular hemorrhage

![Photograph showing dense fibrinous adhesions at the caudal surface of the cerebellum and the brainstem, evident at 9 weeks' survival.](image)

In rats from the H-Tx strain, hydrocephalus develops at 19 to 21 days’ gestation. In a study Jones and Bucknell, H-Tx rats underwent lateral ventricle cannulation, pressure measurement, and constant flow infusion tests from 19 days’ gestation to postnatal Day 21. Between 19 days’ gestation and postnatal Day 10, in the hydrocephalic animals, ventricular CSF pressure demonstrated a small overall rise from 15 to 22 mm H₂O. Between postnatal Days 10 and 21, hydrocephalic animals showed a significant increase in lateral ventricle pressure to 57 mm H₂O. In the hydrocephalic rats, R_out from the lateral ventricles increased from 13.2 mm H₂O/µl/min at 19 days’ gestation to 46.8 mm H₂O/µl/min at 21 days’ gestation, in 65 at postnatal Day 1; there was then no further change to postnatal Day 21. As in our neonatal piglet IVH model, most animal models of chronic hydrocephalus demonstrate an early phase characterized by enlarging ventricles and a slow CSF absorption rate, followed by a prolonged chronic phase during which large ventricles are associated with reduced white matter and cortical thickness, low intraventricular pressure, and an improved CSF absorption rate. In these models, as in our own, the ventriculomegaly persists, with its associated white matter injury, despite a subsequent improvement in CSF absorption. Recruitment of the minor pathways of CSF absorption is likely to play an important role in reducing R_out, particularly in young animals. Although the arachnoid villi represent the classic route for CSF absorption, it is well known that these do not exist in the human neonate. In microscopic studies of autopsy specimens from human fetuses and neonates from 18 weeks’ gestation, no arachnoid villi or granulations were evident before birth. Arachnoid projections appear in the dura around the time of birth, increasing in number throughout childhood. The minor pathways therefore constitute the principal routes of CSF absorption in neonates and include the ventricular ependyma, interstitial and perivascular spaces, and the perineurial lymphatic channels. Flow of CSF through the subarachnoid space of the cranial nerves into the nasal cavity and cervical lymphatic system has been demonstrated in several animal studies. It may represent up to 90% of total CSF absorption. One may speculate that this network may increase in extent in response to a long-term increase in CSF pressure, providing an anatomical substrate for the increase in absorptive reserve several weeks after PHVD. Although we have not been able to confirm this in our piglet IVH and PHVD model, residual blood pigments in the region of the cribiform plate and ventral frontal horns suggest the predominance of bulk CSF flow toward the olfactory nerves.

The timing of neurosurgical interventions to drain CSF in PHVD is inconsistent. Early aspiration of ventricular CSF is likely to reduce ICP and diminish the concentration of toxic inflammatory cytokines in the CSF. Early and aggressive washout of intraventricular blood clot, as demonstrated in DRIFT, has led to improved cognitive outcomes at 2 years. Although the traditional indications for drainage include increasing head circumference, tense anterior fontanel, diastasis of cranial sutures, or neurological deterioration, earlier interventions based on regular ventricular ultrasonography have also been en-

![Photomicrograph of section from area indicated by rectangle in the left panel demonstrating adhesions in the subarachnoid space. H & E, original magnification x20.](image)
courage. In DRIFT, ventricular width 4 mm above the 97th percentile or a combination of anterior horn diagonal width, thalamooccipital distance, and third ventricle width 1 mm above the 97th percentile were used as inclusion criteria; despite these criteria, however, the median age at the time of institution of DRIFT was still 20 days. Early intervention, before reaching 4 mm above the 97th percentile, has been associated with a lower shunt placement rate in a retrospective study. In the ongoing Early versus Late Ventricular Intervention Study (ELVIS), the inclusion criteria have been reduced to any ventricular width over the 97th percentile and a maximum ventricular diagonal width over 6 mm, rather than 10 mm (www.bris.ac.uk/clinicalscienorth/neonatal/ri/phitt.html).

Conclusion

Our study demonstrates that in this neonatal piglet model, derangements of CSF dynamics leading to ventricular dilatation and distortion of periventricular white matter occur early after IVH. Ventricular size does not return to normal despite the improvement in CSF absorption that occurs after several weeks. This supports early and aggressive drainage of intraventricular blood products and CSF in the management of PHVD.

Disclosure

Mr. Aquilina was financially supported by the European consortium “Healthy Aims,” Framework VI. The UK charity Action Medical Research and the Norwegian Research Council supported laboratory staff and equipment.

Author contributions to the study and manuscript preparation include the following. Conception and design: Aquilina. Acquisition of data: all authors. Analysis and interpretation of data: Aquilina, Thoresen. Drafting the article: Aquilina. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Aquilina. Administrative/technical/material support: Chakkarapani, Thoresen.

References


K. Aquilina, E. Chakkarapani, and M. Thoresen
CSF dynamics in neonatal piglet intraventricular hemorrhage


