THERAPY

Current methods in the treatment of posthemorrhagic hydrocephalus in infants

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Abstract

The authors reviewed the most recent methods and approaches in the management of posthemorrhagic hydrocephalus in infants. Posthemorrhagic hydrocephalus in infants is associated with a high mortality and morbidity. The incidence of developmental delay, cerebral palsy, epilepsy end visual impairment in surviving children is variable. All treatments have significant drawbacks. Repeated lumbar punctures are frequently associated with high rate of infection and the amount of cerebrospinal fluid drained may be insufficient. External ventricular drainage appears to be more effective than lumbar punctures in evacuating sufficient volumes of cerebrospinal fluid. With subcutaneous reservoir the withdrawal of a sufficient volume of cerebrospinal fluid is achieved, but intermittent elevations of intracranial pressure still occur.

Intraventricular fibrinolytic therapy is a promising method in the management of posthemorrhagic hydrocephalus, however more studies with larger numbers of patients are needed. The most common treatment of posthemorrhagic hydrocephalus involves permanent ventricular shunting. Shunts with a programmable valve seem to be superior to other shunt systems. In case of compartmentalization endoscopic procedures are preferred. Conservative treatment with acetazolamide and furosemide does not seem to confer any advantage to the management of posthemorragic hydrocephalus. ***(Tab. 2, Fig. 2, Ref. 26.)***

Key words: posthemorrhagic hydrocephalus, drainage, shunting, fibrinolysis, conservative treatment.

Posthemorrhagic hydrocephalus (PHH) represents a serious problem in premature infants. It is associated with high morbidity and mortality. With the improvement in neonatal intensive care, more children with PHH are surviving. Murphy et al. provided evidence that posthemorrhagic ventricular dilation in the 1990s had a more aggressive course than previously (1). This is presumably due to the increasing survival of infants of progressively lower birth weight and gestation followed by improvements in neonatal care (widespread use of antenatal steroids and surfactant).

The incidence of intraventricular hemorrhage (IVH) in very low birth weight infants (VLBW) may be 20–40 %. Posthemorrhagic hydrocephalus occurs in 65–100 % of those with IVH grade III and IV (2). Progressive ventricular dilatation requires temporary or permanent cerebrospinal fluid (CSF) derivation. The incidence of developmental delay, cerebral palsy, epilepsy end visual impairment in surviving children is variable. The outcome in these patients remains limited by the initial brain damage caused by the hemorrhage and accompanying periventricular leukomalacia as well as associated diseases, such as bronchopulmonary dysplasia. The severity of IVH is determined according to Papile's classification (3) (Fig. 1).

Blood in the ventricles commonly occurs as the result of hemorrhage within the subependymal germinal matrix. The subependymal germinal matrix is a richly vascular structure which is most pronounced in the fetus of six to eight months gestation. The matrix is the source of spongioblasts which participate in

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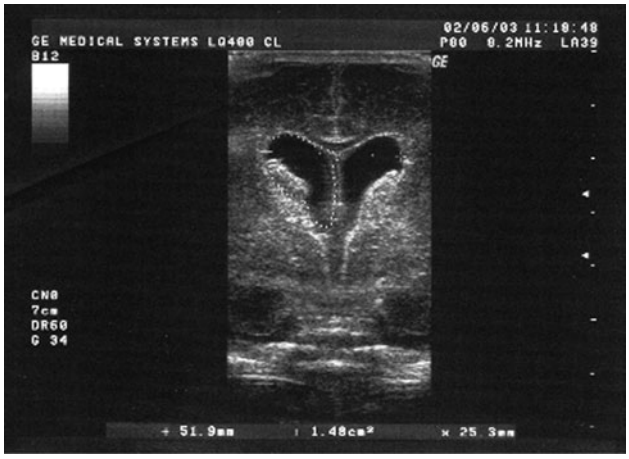

Fig. 1. a: Coronal ultrasonogram of lateral ventricles in a neonate with IVH grade II–III.

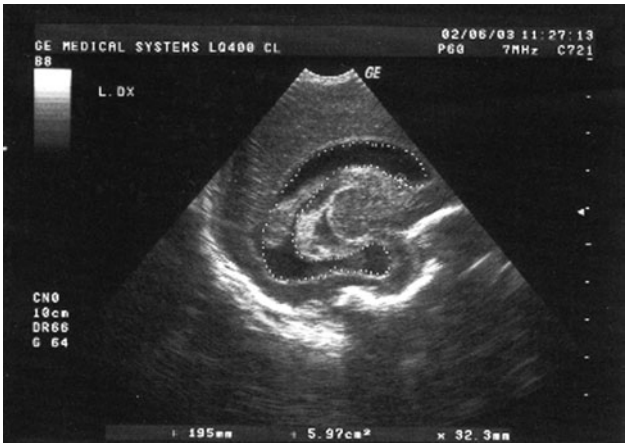

Fig. 1. b: Sagittal ultrasonogram of dilated ventricles in IVH.

the formation of the cerebral cortex, basal ganglia and the other forebrain structures.

The hemorrhage can be isolated or it can rupture through the ependymal lining into the ventricular system. If the hemorrhage is large it may extend into the parenchymal tissue adjacent to the germinal matrix. The majority of hemorrhages occur within the first 72 hours of life.

The development of CSF malabsorption is related to microbstruction of arachnoid villi or to obstruction of CSF pathways, like cisterna magna clots (4). Multiple blood clots may obstruct the ventricular system or channels of reabsorption initially but lead to a chronic arachnoiditis of the basal cisterns involving deposition of extracelullar matrix proteins in the foramina of the fourth ventricle and the subarachnoid space.

Treatment of posthemorrhagic hydrocephalus

There is currently no general agreement on the best way to manage neonatal PHH. All kinds of treatment have significant drawbacks, especially in the VLBW.

Invasive treatment of posthemorrhagic hydrocephalus

Lumbar and ventricular taps

These represent the most common therapeutic approach in the early stages of communicating PHH. The failure of lumbar punctures (LP) may be associated with transformation of communicating PHH into non-communicating because of the obstruction of CSF pathways by blood clots. A considerable rate of infection and the fact that LP is a short lasting method are disadvantaging factors. Using ventricular or lumbar tapping technique, the rate of infections is described to be at about 7–27 % (2, 5). The fact that patients are being submitted to ten or more LPs has to be regarded. The volume drawn at each LP can be different; frequently LPs are just dry taps. For treatment of a high grade bleeding LP seems to be insufficient (6, 7).

External ventricular drainage

After a short series of LPs that prove to be inefficient the external drainage (EVD) is the next invasive step in the management of PHH. The catheter is inserted into the dilated anterior horn of the right lateral ventricle under sterile conditions in the neonatal intensive care unit. The proximal end of the catheter is subcutaneously tunneled to a site on the scalp approximately 1–2 cm from the initial incision and connected to a drainage system. The amount of CSF drained can adjusted by elevating or lowering the level of the drip chamber. EVD appears to be much more effective than repeated LPs in evacuating sufficient volumes of CSF.

The infection rate with EVD ranges from unacceptable levels (8) to very low rates reported by some authors despite long periods with EVD (9, 10). The infection of CSF drainage is regarded as an independent predictive value of poor neurological outcome of the child (2).

Other problems such as overdrainage and the development of subdural hygromas can occur but may be minimized by careful control of intracranial pressure (ICP). EVD also allows easy intrathecal administration of drugs including thrombolytics.

The effect of EVD on shunt dependency and neurological outcome is not known. Long standing EVD may favor subsequent shunt by decreasing natural CSF resorption, on the other hand the need for permanent shunting may be reduced by the continuous removal of bloody and protein rich CSF. The rate of permanent shunting with EVD is 64–68 % (10, 11).

Subcutaneous reservoir

The subcutaneous reservoir (SC) is another frequently used option in the management of PHH. The taps are realized through a subcutaneous reservoir avoiding thus the necessity of ventricular tapping and additional brain injury. Reservoirs are tapped 2–3 times a day, the amount of CSF derived is adjusted to the opening CSF pressure. An important drawback of SCs (and LPs) is that the removal of CSF is intermittent. The fluid buildup and

Fig. 2. Standard Codman Medos programmable valve. The prechamber for puncture and a pumping chamber present advantage in clinical practice.

resulting rise of ICP between taps might be detrimental. The major complications of SC are ventriculitis, shunt infection, skin necrosis, liquor fistula, or subdural hygroma. The rates of infection in SCs reported in the literature are very low (12, 13). Among patients who received a subcutaneous reservoir shunting was necessary in 75–88 % (6, 12, 13, 14).

Intraventricular fibrinolytic therapy

In last decade there have been several reports on the intraventricular administration of fibrinolytics, such as streptokinase or tissue plasminogen activator (tPA) (15, 16).

The proportions of patients requiring permanent VP shunt placement range from 26 % to 100 % (16, 17, 18). Some authors report the same or even higher rates of VP shunt placement with fibrinolytic therapy (16, 18) The reasons for this may be the late intervention when the infants have already developed hydrocephalus.

The timing of the procedure is a factor of major importance. Early intervention probably increases the risk of rebleeding as the bleeding site has not been surgically repaired, in late intervention the pathology may be irrevocably decided with no chance of the intervention altering the course. The therapeutic window for effective treatment with intraventricular fibrinolytic therapy has not yet been identified.

The risk of recurrent hemorrhage appears to be low. The uncertainity is due to the question whether ventricular fibrinolysis alone is sufficient or if subarachnoid fibrinolysis is also required.

Recently Whitelaw and colleagues presented new method involving intraventricular administration of tPA and 72 hours drainage via two ventricular catheters (one frontal on the right, and one occipital on the left) (17). They called this procedure DRIFT (Drainage irrigation and fibrinolytic therapy). The objective was to remove old blood and cytokines. The number of shunt dependent children in their study was low (14 from 19), but this highly invasive and experimental intervention cannot be recommended until a more objective evaluation provides positive evidence.

In the field of intraventricular fibrinolysis we are on a learning curve. Further reports with larger numbers of patients are needed.

Shunting

The permanent drainage of CSF via ventriculoperitoneal (VP) shunts is the most common treatment of PHH. The surgical treatment is still complicated by high revision rates (8, 19). The prematurity of the patients and their relatively incompetent immune system favors shunt infections. The infection rate varies across the studies and is usually between 5–15 %. The infection rate reported by some authors is low especially in last decade. This is probably due to late shunting at the time when CSF is mainly drained from blood and debris and the patient is in a stable clinical condition. According to some reports the infection is unfavorable predictive factor for the neurodevelopmental outcome.

Increased CSF protein levels favor shunt obstructions which are the most common cause of shunt failure in these children (8, 19, 20). The rate of shunt failures according to some reports in ventriculoatrial shunts is higher (9). Physiologically very low ICP levels in premature infants necessitate special shunt systems. For low-birth weight infants low pressure valves or even valveless shunts (21) are recommended by several authors. Low pressure valves usually have to be converted later to medium or high pressure valves, as the ICP increases and the child starts to stand and sit. Shunt overdrainage with collapsed ventricles and eventual subdural fluid collections can occur in children with low pressure valve systems (9, 22). Some authors therefore advocate shunts with programmable valves as the first choice (Fig. 2).

It seems that the clinical outcome does not correlate with the number of shunt complications, but is determined by the primary hemorrhagic lesion (11). The early control of hydrocephalus does not seem to bring about any decisive improvement in the neurodevelopmental outcome of patients with additional intraparenchymal lesions.

The preferable weight for VP shunt implantation is >2000 g.

Compartmentalization occurs frequently in patients with PHH, and subsequent neuroendoscopic procedures or additional shunts are needed. In PHH this seems to be fostered by previous infection or prolonged high levels of blood breakdown products in the CSF. Although repeat endoscopic procedures are necessary in a certain number of cases, the overall revision rate seems less than with additional shunt treatment (23).

There is also controversy about the setting for the surgery. Some authors advocate the neonatal ICU as the most comfortable and safest for patients with PHH. The ICU environment avoids the risks associated with transport of the patient to the operating room (OR), but some report higher infection rates associated with surgeries performed in ICU. Finer et al (24) were the first to demonstrate that the unstable neonate can undergo surgery in the neonatal ICU with a surgical morbidity and mortality comparable to that seen in OR. Transportation does indeed destabilize the already critically ill neonate, because it predisposes to hypothermia, frequently results in dislodgement of intravascular catheters, and is likely to increase postoperative pain.

Non-invasive treatment of posthemorrhagic hydrocephalus

Conservative treatment of PHH consists of peroral or intravenous administration of drugs that reduce CSF production. In the multicentric trial done by Kennedy et al (25) acetazolamide in doses 100 mg/kg/day and furosemide 1mg/kg/day were administered. None of the measures of outcome in this multicentric study suggest any advantage from drug treatment. The International PHVD Drug Trial Group reported the results of randomized controlled trial of acetazolamide and furosemide with the same dose (26). 65 % of infants receiving the drug treatment died or required shunt insertion and 46 % of infants in the control group died or required shunt insertion. 79 % of infants in the drug treatment group were impaired or disabled at 1 year, whereas 53 % of controls were impaired or disabled at 1 year. The CNS infection level was similar in both groups. The trial was stopped by the data-monitoring committee before the planned completion, as the results clearly showed a worse outcome in the drug treated infants.

The rationale for treatment with these drugs is a reduction of the rate of CSF formation, but these drugs had other effects. This has the potential to cause cerebral vasodilatation, impairment of autoregulation, and, thus, cerebral injury. Some data from experimental studies suggest that acetazolamide may be toxic to the developing oligodendrocyte. Alterations in cerebral perfusion pressure therefore may underlie the adverse effects seen in these trials.

For children with PHH, the recognized diagnostic criteria should be used (Tab. 1). Elective use of early repeated lumbar punctures is not recommended. Ventricular taping is not recommended.

EVD provides constant adaptation of the drainage level to the clinical and radiological findings and thus to the apparent needs of the infant. EVD seems to be superior to subcutaneous reservoir tapping. The rate of shunt dependency may be lower with EVD and swings in ICP are avoided. The rate of infection does not exceed that in SCs when appropriately managed. On the other hand the EVD protocol requires careful observation of the infant, sterile technique, gentleness to avoid pain and secondary bleeding and a very accurate CSF balance in addition to the normal demands of intensive care. All this places a heavy responsibility on the nursing stuff.

Fibrinolytic therapy is a promising approach in the treatment of PHH, but the data in comparative studies are difficult to interprete. The numbers of patients are low, the follow-up periods are unequal and the methods of treatment are not standardized. Large, prospective controlled multicenter trials are needed to assess its efficacy.

Acetazolamide and Furosemide are not recommended.

In cases where placement of permanent VP shunt is necessary, programmable valves are preferable. For shunt insertion criteria see Table 2. In non-communicating hydrocephalus neuroendoscopy is superior to shunting.

Tab. 1. Criteria for surgical intervention in PHH.

Ventricular width 4 mm over the 97th percentile	
Symptomatic raised ICP	
Enlargement of head circumference 15 or more mm/week	
Progressive and persistent enlargement of ventricles together with accelerated head enlargement 8–14 mm/week without obvious symptoms	
Over 4 weeks	neurological assessment
Over 6 weeks	evaluation for shunt surgery

Tab. 2. Criteria for shunting in PHH.

CSF protein <2 g/l
Weight>2000g (preferable)
Relapse of ventricular enlargement after EVD removal (not generally accepted)

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