Neuroendoscopic lavage for the treatment of intraventricular hemorrhage and hydrocephalus in neonates

Clinical article

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Object. Neonatal intraventricular hemorrhage (IVH) may evolve into posthemorrhagic hydrocephalus and cause neurodevelopmental impairment. In this study, an endoscopic surgical approach directed toward the removal of intraventricular hematoma was evaluated for its safety and efficacy.

Methods. Between August 2010 and December 2012 (29 months), 19 neonates with posthemorrhagic hydrocephalus underwent neuroendoscopic lavage for removal of intraventricular blood remnants. During a similar length of time (29 months) from March 2008 to July 2010, 10 neonates were treated conventionally, initially using temporary CSF diversion via lumbar punctures, a ventricular access device, or an external ventricular drain. Complications and shunt dependency rates were evaluated retrospectively.

Results. The patient groups did not differ regarding gestational age and birth weight. In the endoscopy group, no relevant procedure-related complications were observed. After the endoscopic lavage, 11 (58%) of 19 patients required a later shunt insertion, as compared with 100% of infants treated conventionally (p < 0.05). Endoscopic lavage was associated with fewer numbers of overall necessary procedures (median 2 vs 3.5 per patient, respectively; p = 0.08), significantly fewer infections (2 vs 5 patients, respectively; p < 0.05), or supratentorial multiloculated hydrocephalus (0 vs 4 patients, respectively; p < 0.01).

Conclusions. Within the presented setup the authors could demonstrate the feasibility and safety of neuroendoscopic lavage for the treatment of posthemorrhagic hydrocephalus in neonates with IVH. The nominally improved results warrant further verification in a multicenter, prospective study.

Key Words • endoscopic lavage • hydrocephalus • neuroendoscopy • intraventricular hemorrhage • neonates • premature infants

Posthemorrhagic hydrocephalus after intraventricular hemorrhage (IVH) remains a challenge in the treatment of newborn infants, most of whom are born prematurely. Despite ongoing medical progress, a significant number of premature infants continue to suffer from IVH and the potential sequelae of primary brain damage as well as permanent disturbed CSF circulation, which may necessitate lifelong treatment with CSF diverting devices.

Attempts to manage IVH have aimed to reduce the rate of children in need of permanent CSF diversion and to improve neurodevelopmental outcome. One reported approach was directed toward the removal of an intraventricular hematoma via application of a fibrinolytic agent and irrigation of the ventricular system.²⁵–²⁷ Although recruitment to the randomized controlled setup of this approach was discontinued because of increased rates of rehemorrhage and failure to reduce the rate of shunt dependency within the treatment group, long-term outcome after 2 years was superior in the treatment group, with reduction of the rate of death and severe disability. Taking these data into account, it was hypothesized that if a more controlled technique could be applied, fewer complications of secondary hemorrhage might be caused, but a similar long-term outcome might be achieved. Two factors may have contributed to the increased secondary hemorrhage rates, and if avoided, may allow safe removal of intraventricular blood components. First, externalized irrigation over several days may have allowed only limited control for inflow, outflow, and intracranial volume balance. Second,
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the use of fibrinolytic agents may increase the risks for further hemorrhage. Therefore we favor a time-limited, minimally invasive endoscopic approach to perform the irrigation under controlled and sterile conditions, as suggested previously.6 Furthermore, we aimed to avoid any additional drug components and exclusively used warmed Ringer solution. This paper describes the approach of neuroendoscopic lavage for the treatment of hydrocephalus following IVH in newborns and compares the results to our historic controls treated conventionally.

Methods

Study Population

All consecutive patients who were diagnosed with an IVH with or without concomitant intraparenchymal hemorrhage, and who subsequently underwent an operation by neuroendoscopic lavage for signs of disturbed CSF circulation, were retrospectively identified using the hospital's database for surgical procedures. These patients were operated on between August 2010 and December 2012 (29 months). For a similar time period of 29 months (March 2008 to July 2010), prior to changing our treatment protocol, all patients with the same clinical condition treated using a conventional protocol were also identified.

General Treatment

From 2008 to 2012, all infants admitted to the neonatal service of our hospital were routinely screened with cranial ultrasonography (GE Vivid 7 Dimension, GE Healthcare Biosciences). If an IVH was documented, these infants were further followed with daily recordings of head circumference and serial cranial ultrasonography examinations every second day. During these examinations, standard parameters of ventricular dimension were recorded, including ventricular index (VI), anterior horn width (AHW), thalamo-occipital distance (TOD), and third ventricle width (TVW).

Indications for surgical intervention in both groups were signs of disturbed CSF dynamics: abnormally enlarging head circumference (more than 2 mm per day, averaged over 1 week), or progressive ventricular dilation determined by ultrasonography (VI > the 97th percentile + 4 mm, AHW > than the 97th percentile + 1 mm, TOD > the 97th percentile + 1 mm, and TVW > the 97th percentile + 1 mm) in combination with clinical signs (such as bulging fontanel, vomiting, bradycardia, and others).

Surgical Treatment

Prophylactic antibiotics were routinely given to all patients, initially flucloxacillin at 50 mg/kg, and since 2010, cefuroxim at 50 mg/kg. The patient was positioned supine with the head fixed in a vacuum mattress. Patients in the conventional treatment group were treated with temporary CSF diversion. This was performed either by the neonatologists with intermittent lumbar or ventricular punctures, or by neurosurgical interventions with an implanted ventricular catheter connected to either an external CSF drainage system (external ventricular drain) or a subcutaneously placed bur hole reservoir (ventricular access device). In brief, for the neurosurgical procedures, a small semicircular skin incision was made in the respective frontal area approximately 1 cm in front of the coronal suture in the midpupillary line. This anatomical location—in contrast to access through the fontanel—was chosen to firmly fix the implanted reservoir over the bone. A pinpoint bur hole was achieved by rotating a no. 15 scalpel and was further enlarged with a rongeur. The dura was coagulated and incised to facilitate passing of the ventricular catheter into the frontal horn. The implanted ventricular catheter was connected to a bur hole reservoir (Miethke-Aesculap) or tunneled subcutaneously in cases of external ventricular drain implantation.

In patients in whom a neuroendoscopic lavage was performed, the ventricle with the larger amount of hematoma was punctured with the endoscopic unit (Minop System, Aesculap) under intraoperative ultrasound guidance, as described previously.21 Once the ventricle was entered, continuous irrigation was started with warmed (37°C) lactate-free Ringer solution, which was established by passive inflow via an infusion system through the irrigation channel of the endoscopic unit. Simultaneously, a passive outflow was ensured through the unit’s second channel to balance the intracranial volume and avoid any significant changes in intracranial pressure. Continuous irrigation allowed orientation along landmarks and identification of the clotted hematoma. The hematoma was usually attached either along the course of the choroid plexus or as a mass along the anterior lateral ventricular wall and the head and body of the caudate nucleus. In addition to passive irrigation, active aspiration was performed by repeatedly bringing the outflow port of the endoscopic unit in proximity to the hematoma and by applying moderate suction with a connected syringe, thereby gently reducing the clotted blood portions. This maneuver was withheld if the clot was firmly attached to the choroid plexus or the parenchymal ventricular walls. The third ventricle—where the clot might be attached to the choroid plexus along the roof—was entered to remove possible free-floating hematoma clots by aspiration and to ensure the patency of the aqueduct. Using an interventricular septostomy, similar irrigation and aspiration of the hematoma within the contralateral ventricle was performed. Irrigation was stopped once the fluid within the ventricular system was clear to allow a thorough inspection, and no larger accessible parts of the coagulated hematoma remained (Fig. 1). Typically, 2000–3000 ml of Ringer solution was used for such a procedure. After removal of the endoscope, a ventricular catheter connected to a subcutaneous bur hole reservoir was placed to allow possible later CSF aspiration. The corticotomy tract around the ventricular catheter was sealed with a gelatin sponge. After fixation of the reservoir by adapting the periosteam over the reservoir, a standard 2-layer closure of the skin was performed.

Postoperatively, all patients were transferred to the neonatal intensive care unit or intermediate neonatal care unit. Antibiotics were routinely given for 24 hours. Head circumference was recorded daily, and ultrasonography was performed every second day. In cases of continued signs of active hydrocephalus with progressively and abnormally enlarging head circumference, or a combination
of progressively enlarging ventricular size at serial ultrasonography examinations and clinical signs (such as bulging fontanel, poor feeding, vomiting, bradycardia, or apnea), the implanted bur hole reservoir was tapped and CSF was withdrawn (approximately 10 ml/kg of body weight). If the ultrasound at that time point demonstrated a significant amount of residual intraventricular hematoma in the previously endoscopically treated patients, a repeat neuroendoscopic lavage was performed prior to starting CSF punctures. The frequency of these punctures was adjusted to the clinical situation, but punctures were usually performed every 2–3 days. If an external ventricular drain was placed, it was left open for drainage at a level of 10 cm H₂O above the external acoustic meatus. Prophylactic antibiotics (flucloxacillin or cefuroxime) were administered.

The decision to implant a permanent ventriculoperitoneal (VP) shunt was made if serial punctures or continuous CSF drainage via the external ventricular drain failed to arrest the clinical signs of active hydrocephalus. The criteria for shunt placement were equivalent to the first surgical intervention in terms of enlarged head circumference or ventricular enlargement in combination with clinical signs once the CSF protein concentration was less than 2 g/L and the patient should have reached a minimum weight of 1800 g.

During a VP shunt insertion the frontal wound was reopened and the intraventricular catheter was exchanged. An adjustable differential pressure valve with a gravitational unit (proGAV, Miethke-Aesculap) was implanted retroauricularly. All shunt catheters are impregnated with antibiotics (rifampicin and clindamycin; Bactiseal, Codman). In addition, intravenous antibiotics were routinely given for 24 hours perioperatively. Postoperative care after VP shunt insertion was similar as above with clinical examinations, serial measurements of head circumference, and regular ultrasonography. Discharge from the hospital was arranged after interdisciplinary consensus was reached with the patient’s respective neonatologist.

Postoperative Follow-Up

After discharge, all patients were routinely evaluated in both a neonatal and a pediatric neurosurgical outpatient clinic, monthly for the first 3 months, and then every 3 months until the completion of the first year of life. At follow-up appointments the child was clinically assessed, the head circumference was recorded, and an ultrasonography examination was performed. Explantation of the bur hole reservoir and ventricular catheter (if not converted to a VP shunt) was performed after 1 year at the earliest, according to the parent’s preference.

Statistical Analysis

Statistical calculations were performed with GraphPad Prism software (version 5.0f for Mac OS X, GraphPad Software). Categorical data from contingency tables comparing the 2 study groups were evaluated by the 2-sided Fisher exact test. A 2-tailed Mann-Whitney U-test was used to evaluate the differences between continuous data in both study groups. A 2-tailed Wilcoxon matched-pairs signed-rank test was used to evaluate the differences be-
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twix the pre- and postoperative radiological data. A p value < 0.05 was considered statistically significant.

**Results**

**Patient Characteristics**

During the first half of the observation period (March 2008 to July 2010) 10 patients were treated for the development of posthemorrhagic hydrocephalus. At first surgery a bur hole reservoir was implanted in 5 patients, and 3 patients with CSF diversion via an external ventricular drain were transferred from outside hospitals. The remaining 2 patients were treated with serial lumbar or ventricular punctures. During the observation period from August 2010 to December 2012, 19 patients underwent a neuroendoscopic procedure with irrigation of the ventricular system and aspiration of intraventricular hematoma. There were no significant differences in patient characteristics between groups (Table 1).

**Radiological Data**

The ventricular dimensions prior to the first intervention were reviewed for both groups. All indices (VI, AHW, TOD, and TVW) were significantly increased compared with the respective age-adapted norms immediately prior to the first operative intervention (Fig. 2). In the preoperative parameters, significantly larger parameters of ventricular width were observed in the conventional group compared with the neuroendoscopic group: median VI 23 mm vs 19 mm, respectively; median AHW 20 mm vs 18 mm, respectively; and median TOD 30 mm vs 40 mm, respectively. One week after endoscopic lavage some of the ventricular parameters were significantly decreased: from a median of 18 mm (range 12–31 mm) to 15 mm (range 8–29 mm) for AHW (p < 0.01), and from 30 mm (range 19–58 mm) to 28 mm (range 15–49 mm) for TOD (p < 0.05). For VI and TVW, no statistically significant reduction was observed, from a median VI of 19 mm (range 14–38 mm) to 18 mm (range 12–34 mm; p = 0.23), respectively, and from a median TVW of 10 mm (range 4–19 mm) to 7 mm (range 2–19 mm; p = 0.10), respectively. In contrast, such an effect was not observed in the conventional treatment group, in which no statistically significant difference in the ventricular dimensions before and after the initial temporary CSF diversion was noted: median VI 23 mm (range 9–39 mm) after the procedure (p = 0.92); median AHW 20 mm and 21 mm, respectively (ranges 3–42 mm and 4–36 mm, respectively; p = 0.93); median TOD 40 mm and 41 mm, respectively (ranges 17–52 mm and 10–56 mm, respectively; p = 0.23); and median TVW 9 mm and 10 mm, respectively (ranges 4–20 mm and 2–40 mm, respectively; p = 0.10).

**Shunt Insertion Rate**

All patients in the conventional treatment group pro-

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<tr>
<td>no. of patients</td>
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<td>19</td>
<td>0.63</td>
</tr>
<tr>
<td>gestational age at birth</td>
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<td></td>
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<td>median in wks + days</td>
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<tr>
<td>weight at birth (g)</td>
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<td>1036</td>
<td>0.96</td>
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<tr>
<td>range in wks + days</td>
<td>564–3260</td>
<td>520–3460</td>
<td></td>
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<tr>
<td>IVH Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1</td>
<td>2</td>
<td></td>
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<tr>
<td>III</td>
<td>8</td>
<td>13</td>
<td></td>
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<tr>
<td>IV</td>
<td>3</td>
<td>3</td>
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<td>gestational age at first intervention</td>
<td></td>
<td></td>
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<td>median in wks + days</td>
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<td>weight at first intervention (g)</td>
<td>1870</td>
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<td>range</td>
<td>1105–3260</td>
<td>750–3645</td>
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<tr>
<td>gestational age at shunt insertion</td>
<td></td>
<td></td>
<td>0.72</td>
</tr>
<tr>
<td>median in wks + days</td>
<td>37 + 5</td>
<td>37 + 2</td>
<td></td>
</tr>
<tr>
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<td>weight at shunt insertion (g)</td>
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<td>3090</td>
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<tr>
<td>range</td>
<td>2375–4175</td>
<td>2160–7200</td>
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gressed to demonstrate signs of active hydrocephalus and underwent serial and intermittent CSF withdrawal. For patients with implanted reservoirs or those patients treated with lumbar or ventricular punctures, the median number of required punctures was 9 (range 6–11 punctures; Table 2). All patients required insertion of a VP shunt (a 100% shunt placement rate). The median interval between first intervention and VP shunt insertion in this group was 2 weeks and 5 days (range 2 weeks and 0 days to 13 weeks and 5 days).

Of the 19 patients who underwent neuroendoscopic lavage, 11 subsequently continued to show signs of active hydrocephalus requiring serial tapping of the reservoir (median number of punctures = 2, range 1–6). The number of required punctures prior to shunt insertion only in those patients was significantly fewer than in the conventional group (p < 0.01). None of these patients showed resolution of disturbed CSF circulation and required insertion of a VP shunt, resulting in a shunt rate of 58% in the neuroendoscopic lavage group, which was significantly lower than in the conventional treatment group (p < 0.05). Most of the patients who required a shunt experienced a prolonged stable interval and only later deterioration of CSF dynamics, which is reflected in the longer median interval between neuroendoscopic lavage and VP shunt insertion of 6 weeks and 0 days (range 3 weeks and 2 days to 29 weeks and 6 days) as compared with a median of 2 weeks and 5 days (range 2 weeks and 0 days to 13 weeks and 5 days; p = 0.16) in the conventional group (Table 2).

Repeat Procedures and Complications

Conventional Treatment Group. Four of the patients in the conventional treatment group developed a CSF infection prior to the insertion of the VP shunt necessitating further early operative revisions. After the VP shunt insertion, 1 further infection occurred. Four patients developed a supratentorial multiloculated hydrocephalus, which necessitated further surgical revisions. In 1 patient, the VP shunt had to be converted to a ventriculoatrial shunt due to postinfectious abdominal pseudocyst formation. The total number of necessary procedures was 43 operative procedures (median 3.5 procedures per patient, range 1–11 procedures) within the first 12 months (Table 2; Fig. 3 upper).

Neuroendoscopic Treatment Group. No immediate complications were observed after the initial endoscopic procedure. There were no cases of recurrent hemorrhage, hygroma formation, CSF leakage, or postoperative infection after the endoscopic procedure. Four (21%) of the patients who had undergone a neuroendoscopic lavage underwent a repeat neuroendoscopic procedure. The indication for repeated neuroendoscopic lavage was estab-
lished because the above-mentioned criteria of active hydrocephalus were met and the cranial ultrasound documented accessible, residual contralateral hematoma. All those patients were treated in the first half of this series. Three patients underwent additional procedures prior to shunt insertion: 1 transaqueductal stent was placed for a developed isolated fourth ventricle 10 weeks and 3 days after the endoscopic procedure, and 1 third ventriculostomy was performed for clinical and radiological signs of triventricular hydrocephalus due to aqueductal stenosis at 19 weeks and 1 day after the initial procedure. Both patients subsequently required VP shunt insertion at 14 weeks and 1 day, and 29 weeks and 6 days, after the initial endoscopic lavage. One further patient was initially discharged after an uneventful neuroendoscopic lavage and postoperative course. He was admitted overnight with signs of active hydrocephalus 2 weeks and 2 days after the neuroendoscopic lavage when an external ventricular drain was placed. This drain was converted into a shunt during the following days.

Of the 11 patients who had a VP shunt inserted after the initial endoscopic approach, 6 required surgical revisions during follow-up. There were 2 infectious complications necessitating explantation of the shunt, temporary CSF diversion via an external ventricular drain, and reinsertion of a shunt following systemic, calculated antibiotic treatment. In 2 patients an obstructed valve had to be exchanged. The total number of necessary operations was 47 procedures (median 2.0 per patient, range 1–7 procedures) within 12 months. The total number of necessary surgeries in the endoscopic treatment group was not significantly lower as compared with the conventional group (p = 0.08). None of the patients in this group developed a supratentorial multiloculated hydrocephalus (Table 2; Fig. 3 lower).

The timing of the initial endoscopic procedure as a possible factor for later shunt dependency was examined. The mean time after the initial hemorrhage for patients in whom a neuroendoscopic lavage succeeded in preventing later shunt insertion was 19 ± 11 days. In patients in whom neuroendoscopic lavage failed to prevent later shunt insertion, the time between hemorrhage until surgical intervention was 22 ± 7 days, which was not significantly different (p = 0.40). Furthermore, no significant relationship between IVH grade and the need for shunt insertion could be demonstrated (p = 0.74).

### Discussion

Prematurity remains a challenging situation in the care of newborn babies. Among other well-known complications, IVH and subsequent posthemorrhagic hydrocephalus continue to have a significant impact on the developmental potential of the child. Although perinatal morbidity has decreased over time, the rate of severe IVH (Grades III and IV) remains approximately 3%–20% in prematurely born babies with very low birth weight.3,10,20 Approximately 29% to 49% of the neonates with IVH Grades III and IV will develop posthemorrhagic ventricular dilation necessitating treatment.3,44 Once temporary treatment is initiated, 38%–92% of those patients will subsequently require permanent shunt placement.10,17,24,25

Conventional treatment options consist of repeated and intermittent CSF withdrawal via lumbar puncture or a ventricular access device. Alternatively, continuous CSF drainage via an external ventricular drain or a subgaleal shunt can be employed. Attempts to decrease CSF production by the administration of acetazolamide and furosemide demonstrated no beneficial effect on outcome.12

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**TABLE 2: Results of treatment in each patient group**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>no. of patients</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>necessary CSF punctures prior to shunt insertion</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>median</td>
<td>6–11</td>
<td>1–6</td>
</tr>
<tr>
<td>range</td>
<td>6–11</td>
<td>1–6</td>
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<tr>
<td>time to shunt insertion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>median in wks + days</td>
<td>2 + 5</td>
<td>6 + 0</td>
</tr>
<tr>
<td>range in wks + days</td>
<td>2 + 0 to 13 + 5</td>
<td>3 + 2 to 29 + 6</td>
</tr>
<tr>
<td>VP shunt rate (%)</td>
<td>10/10 (100)</td>
<td>11/19 (58)</td>
</tr>
<tr>
<td>operations/patient in 12 mos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>total operations</td>
<td>43</td>
<td>47</td>
</tr>
<tr>
<td>median per patient</td>
<td>3.5</td>
<td>2</td>
</tr>
<tr>
<td>infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>% per total number of procedures</td>
<td>11.6</td>
<td>4.3</td>
</tr>
<tr>
<td>multiloculated hydrocephalus cases</td>
<td>4/10</td>
<td>0/19</td>
</tr>
<tr>
<td>isolated 4th ventricles</td>
<td>1</td>
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Because the development of posthemorrhagic hydrocephalus starts with the initial hemorrhage, the removal of the intraventricular hematoma as the causative agent may be a possible treatment option. This method has been established for the treatment of adult IVH and was investigated in previous studies for newborn premature babies as well. The most detailed approach thus far consists of insertion of a frontal and a contralateral occipital ventricular catheter. After instillation of recombinant tissue plasminogen activator and short clamping, the ventricular system was continuously irrigated for a median period of 3 days. Although demonstrating a reduced rate of later shunt insertion in the pilot study, this effect could not be repeated in a later randomized trial of drainage, irrigation, and fibrinolytic therapy for premature infants (DRIFT study) in which no reduction of subsequent shunt surgery or death was observed after 6 months of follow-up. In this study, a 34% rebleeding rate was noted within the DRIFT group and recruitment was discontinued. Despite this adverse effect of increased rehemorrhage, the DRIFT-treated infants demonstrated a better neurological state after a follow-up of 2 years, with reduced severe cognitive disability in survivors and a lower overall death or severe disability rate. This series of DRIFT studies constitutes the background for the data presented in this paper. The presented surgical approach was chosen to avoid
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the sequelae reported in the DRIFT study. Neuroendoscopic lavage is a controlled and time-limited procedure in the safe setting of the operating theater with trained staff, intraoperative monitoring, and sterile conditions. Furthermore, this surgical technique offers direct visualization of the progress of hematoma removal and control of possible bleeding sites, which constitutes a valuable advantage. During the procedure, strict control of intracranial volume is assured and irrigation can be directed toward accumulated, free-floating degradation products of the hematoma, while residual clots may be removed by visually controlled active aspiration within the supratentorial ventricular system, with the exception of the temporal horns. All these factors represent advantages in comparison with the DRIFT protocol, in which a hemolytic agent is initially used and the ventricular system is passively perfused over days on a neonatology unit. Consequentially, no cases of rehemorrhage were observed after an endoscopic lavage during the postoperative follow-up. As a result of the presented data without significant surgical complications immediately after endoscopic lavage, it is reasonable to conclude that this procedure is feasible and safe in a neuroendoscopically experienced team.

Despite the fact that the group size was small in both the conventionally and endoscopically treated patients, statistically significant differences could be observed. The comparison of pre- and postoperative ultrasonography demonstrated that a significant reduction of the ventricular size after 1 week in the neuroendoscopic lavage group was not noted in the conventional group. Furthermore, the amount of necessary punctures after the first procedure was significantly lower in the endoscopic treatment group. The overall shunt rate was significantly reduced from 100% to 58%, while the number of necessary surgical interventions was not significantly lower in the endoscopically treated group. The shunt placement rate after posthemorrhagic ventricular dilation after severe IVH (Grades III and IV) varies between 38% to close to 100% in the literature, and reported institutional rates can be quite different from both of the groups described in our study.

Caution must be applied when comparing reported shunting rates in the literature because of different baseline patient characteristics, such as shunt rate in relation to a group of all prematurely born children, versus a group of all patients diagnosed with any IVH, versus a group of patients with only Grade III and IV IVH. A further possible explanation is the differing treatment algorithms and the differing indications for shunt insertion. When deciding on shunt implantation, all involved medical specialties have to balance the commitment to a lifelong implant with potential surgical revisions throughout a patient’s life with the fact that an untreated active hydrocephalic state causes marked loss of cerebral parenchyma with detrimental consequences for future development. For this study, it is important to emphasize that neither the indication for any primary intervention and possible subsequent shunt insertion, nor the team of neonatologists and pediatric neurosurgeons, was changed over the observation period, which bolsters the conclusion that neuroendoscopic lavage beneficially reduced the need for later shunt insertion in our specific setting. Furthermore, a beneficial effect regarding the overall number of necessary surgical procedures was demonstrated. Given the fragile condition of this patient population, this appears to be an important finding and an advantage of the endoscopic approach. Also, the rate of infections was significantly lower in the neuroendoscopy group. One possible explanation would be the amount of CSF punctures, which was significantly lower in the neuroendoscopic group. Consequently, the rate of multiloculated hydrocephalus, which is often triggered by previous infections, was significantly decreased in the neuroendoscopy group. This is a relevant finding because multiloculated hydrocephalus and an isolated fourth ventricle constitutes a complication that often necessitates multiple operative interventions. The removal of intraventricular blood may diminish the inflammatory reactions to blood degradation products. This inhibition of the inflammatory process might thereby decrease the rate of multiloculated hydrocephalus, as well as any direct negative effect on brain development.

The discussed results after neuroendoscopic lavage of decreased ventricular dimensions, shunt rate, infection, and supratentorial multiloculated hydrocephalus rate demonstrate the efficacy of the endoscopic approach on limited scientific grounds, because the historical control group includes unavoidable flaws in study design. However, for this study we attempted to compare the recent standardized procedure of neuroendoscopic lavage to the rather diverse protocol of the conventional treatment group to prove safety and feasibility, but also to get an idea about possible efficacy of this neuroendoscopic procedure. The latter needs further efforts to be investigated in a prospective multicenter study. In addition, it is essential to further elucidate the neurodevelopmental outcome in this cohort similarly to the 2-year outcome of the DRIFT study and evaluate follow-up MR images to assess any structural brain shape changes, such as possible porencephaly at the site of the intervention.

The period until a shunt was inserted showed a trend of being longer in the endoscopic lavage group compared with the conventional treatment group. We observed a common pattern in patients who eventually required shunt insertion after neuroendoscopic lavage: an initial period of clinical stability over several days, during which no CSF punctures were necessary, followed by slow reactivation of the hydrocephalus and further need of additional CSF withdrawal. By that time, the CSF characteristics and the patients’ weights and conditions allowed timely insertion of a shunt. In contrast, repeated CSF punctures were necessary early on and throughout the whole period in the conventional treatment group. Of note, also in the neuroendoscopic treatment group, we did not observe a single patient who required later CSF withdrawal and did not progress in hydrocephalic activity toward shunt dependency. Cerebrospinal fluid withdrawal by repeatedly tapping a reservoir did not lead to resolution of a posthemorrhagic hydrocephalus in either of our patient groups. Tapping and CSF withdrawal could only be used as a transient and intermittent measure rather than an effective intervention to clear the ventricular system or to stop progression toward shunt dependency in our patients.

Previous investigations for posthemorrhagic hydrocephalus considered the timing of intervention an impor-
tant factor for outcome, suggesting that an earlier intervention might be beneficial. We analyzed our data as to whether earlier intervention with neuroendoscopic lavage was associated with shunt independence. We could not show a clear trend toward later intervention and concomitant later shunt dependency, but low sample sizes in this respect warrants further investigation to clarify this factor. Whether an earlier neuroendoscopic lavage will avoid later shunt dependency, especially to a higher degree, should be addressed in further investigations, particularly in view of the markedly enlarged ventricular dimensions of both groups at the time of the first intervention in this study.

Potential limitations of the current study include the study design comparing historical controls to the recent treatment regimen, the small patient sample sizes, and any selection bias (because some of the patients of the conventional group were referred to our service with an established infection, thereby increasing the infection rate in the conventional group). Similarly, we observed that more patients were referred to our institution since the endoscopic approach became a possible treatment option within the region, explaining the different group size. Although the 2 groups did not statistically differ with regard to their baseline characteristics, the conventional treatment group had slightly but significantly larger ventricular parameters at the first intervention, which might have had an adverse effect on later shunt rate. We assume that timing of the primary intervention is one factor with an influence on later shunt rate among others, such as initial amount of intraventricular blood, amount of residual blood degradation products after an intervention, or the presence of an infection. The presented groups are obviously too small to meaningfully attempt to weight these factors against each other. Taking those limitations into consideration, we are able to prove the technical feasibility and safety of endoscopic lavage and to demonstrate a nominally improved outcome in comparison with our available historical control group.

Conclusions

The presented data document that the well-tolerated neuroendoscopic lavage is a feasible technique to remove intraventricular blood degradation products and residual hematoma in neonates suffering from posthemorrhagic hydrocephalus. The safety and feasibility of this approach was documented by the absence of any significant procedure-related complications within the early postoperative phase. The nominally improved outcome of the neuroendoscopic group in comparison with historical controls with a significantly lower shunt rate and significantly fewer complications indicates evidence of this approach’s efficacy that warrants validation in an appropriately powered prospective randomized trial.

Disclosure

Dr. Thomale receives travel funds from B. Braun Aesculap and is reimbursed as a lecturer.

Author contributions to the study and manuscript preparation include the following. Conception and design: Thomale, Schulz.

References

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