Neural tube defects are common in East Africa relative to more developed regions of the world, due at least in part to high birth rates and a lack of maternal and perinatal care, including folic acid supplementation and prenatal diagnosis. Hydrocephalus develops in a substantial number of these children, with a reported incidence rate as high as 80–90%. A significant rate of shunt failure occurs before 6 months in 86% of the patients, and none occurred after 10 months. The operative mortality rate was 1.1%, and there were no infections. Life table analysis suggested that 72% of the patients would be successfully treated using a single ETV-CPC and 78% would remain shunt-independent with opening of a closed ETV stoma. Multivariate logistic regression showed scarring of the cistern (p = 0.021) or choroid plexus (p = 0.026) as predictors of failure, but age at the time of surgery was not a significant predictor.

Conclusions. Using ETV-CPC appears to successfully provide a more durable primary treatment of hydrocephalus for infants with spina bifida than does shunt placement. These results support ETV-CPC as the better treatment option for these children in developing countries. (DOI: 10.3171/PED.2008.2.11.310)

**Key Words** • choroid plexus cauterization • developing world • endoscopic third ventriculostomy • hydrocephalus • myelomeningocele

Abbreviations used in this paper: CP = choroid plexus; CPC = CP cauterization; CSF = cerebrospinal fluid; ETV = endoscopic third ventriculostomy; VPS = ventriculoperitoneal shunt.
can typically be managed emergently so as to avoid patient morbidity and death.

The situation is very different in developing regions of the world such as East Africa. Shunt-dependency is more dangerous in less developed countries where no patient safety net exists that can provide reasonable access to urgent treatment for shunt malfunction. This absence of a safety net results from a lack of neurosurgeons (an overall ratio of more than 10,000,000 people—about half of them children—per neurosurgeon in the countries of East Africa), poverty that inhibits travel and payment for care, as well as poor infrastructure and regions of insecurity that further impede the ability to travel, especially during the night. Therefore, finding effective treatment alternatives to shunt placement is particularly important for these patients.

At CURE Children’s Hospital of Uganda, we found that combining CPC with ETV was more successful than using ETV alone for treating hydrocephalus in infants < 1 year of age. Among 423 infants < 1 year of age undergoing primary endoscopic treatment of hydrocephalus, 209 were treated with ETV alone, with a 47% success rate, and 214 were treated by combining ETV and CPC, with a 66% success rate (p < 0.0001). The mean follow-up in this study was 19 months for those undergoing ETV alone and 9.1 months for those undergoing the ETV-CPC procedure. The advantage of the combined procedure was most pronounced for infants with hydrocephalus associated with myelomeningocele. In this group, the success rate for ETV alone was 35%, whereas ETV-CPC was successful in 34 (76%) of 45 patients (p = 0.0045). The current study extends the initially reported experience with using ETV-CPC as the primary treatment for spina bifida–related hydrocephalus, and reports results from a larger group of East African infants with a longer follow-up duration.

Methods

After closure of the patient’s myelomeningocele, infants were monitored for the development of hydrocephalus using serial head circumference measurements, evaluation of anterior fontanel tension, and head ultrasonography or CT scanning to assess for increasing ventricular volume. Patients were only treated when progressive hydrocephalus was evident.

The technique for the combined ETV-CPC procedure has been described previously, as have the special technical considerations and anatomical variations of intraventricular anatomy in these patients. A flexible endoscope (model 11282 BN), telecom (model SL pal 20212020), xenon nova light source (model 20131520), and Bugby electrocautery wire (all from the Karl Storz Co.), and a Sony Trinitron monitor (model PVM-14N5MDE, Sony Corp.) were used. The details of endoscope and camera sterilization, operative setup, and ventriculoscopy procedure used in the setting of Uganda have been previously reported.

Infants with hydrocephalus in association with myelomeningocele and a Chiari malformation Type II harbor a spectrum of common intraventricular anatomical variations that can increase the technical challenge of performing the ETV, especially for those surgeons less experienced in ventriculoscopy. These variations, reported previously, include a thick third ventricle floor; tissue bridges that span the third ventricle walls or cross within the floor of the third ventricle; enlarged massa intermedia (interthalamic adhesion); aqueductal stenosis; stenosis or atresia of the foramina of Monro; an incomplete or absent third ventricle roof; fused, thickened fornical columns; absent septum pellucidum; and a mobile glomus choroidae that is tethered to the choroidal fissure by an expansive, redundant fibrovascular membrane.

Endoscopic Third Ventriculostomy Procedure

After the induction of general endotracheal anesthesia, the patients were positioned supine with their head turned to the left and prepared as if they were undergoing a right frontal VPS placement. This preparation was performed so as to facilitate shunt placement in the event of technical failure while performing the ETV. A curved incision was made in the right lateral corner of the anterior fontanel to create a small scalp flap centered on the midpupillary line. The dura was opened sharply with a No. 15 blade to facilitate its primary closure at the conclusion of the procedure. After coagulating the cortical surface and penetrating it with the trochar of a 14 Fr introducer sheath, the endoscope was inserted into the right frontal horn and maneuvered into the third ventricle.

After inspecting the aqueduct and the anatomy of the ventricular floor, the site for the ETV was determined. Typically the basilar apex was not visible through the thick floor, and often there were no distinguishable mammillary bodies. The Bugby wire was used to gently depress the floor ~ 2–3 mm behind the infundibular recess to determine the location of the underlying dorsum sellae. It was common for a tissue bridge to further thicken the floor at that point, and the ETV was usually created immediately anterior to this bridge. The ventricular floor was then penetrated bluntly with the Bugby wire but without the use of any electrocautery. This latter point is very important in avoiding basilar artery injury. With gradual penetration of the floor, the dorsum sellae and the Lilliequist membrane came into view. Upon penetration of the Lilliequist membrane, the endoscope was threaded over the wire into the prepontine cistern. An unobstructed view of a naked basilar artery and its branches as well as the cranial nerves was sought to confirm entry into the cistern. The scope was then withdrawn back into the ventricle and flow was noted across the Lilliequist membrane fenestration and the ETV ostium.

Choroid Plexus Cauterization Procedure

Next, the CPC procedure was addressed. Beginning at the right foramen of Monro, the Bugby wire monopolar electrocautery was used to cauterize the CP beginning at the right foramen of Monro, and following it back to the typically mobile glomus choroidae in the atrium. After completing this portion of the cauterization, the scope was advanced posteriorly past the atrium, and then manipulated into the right temporal horn by twisting the endoscope between the right thumb and forefinger and simultaneously flexing the tip by manipulating the control lever with the left hand. In this way, access was gained to
the extremity of the CP in the temporal horn, as shown in Fig. 1A. Following completion of the CPC in the right lateral ventricle, the procedure was repeated in the left lateral ventricle. If the septum pellucidum was intact, a septostomy was performed to gain access to the contralateral ventricle. If the septum pellucidum was intact, a septostomy was performed at a site superior to the posterior margin of the foramen of Monro and in an area avoiding any visible veins. The Bugby wire was used to cauterize a circular area and then to penetrate both leaves of the septum. The septostomy was then widened by applying gentle traction to its margins and the scope was passed into the left lateral ventricle where the CP typically came immediately into view (Fig. 1B–D).

Throughout the procedure, intermittent irrigation using lactated Ringer solution and gentamicin solution was used. After the CPC, the ETV stoma was inspected again to insure its patency, and the scope was withdrawn. The dura and galea were closed with 4-0 Vicryl sutures, and the skin edges were sealed with locally obtained glue (cyanoacrylate).

Postoperative Follow-up and Statistical Analysis

Generally, the patients were followed-up at ~1, 3, 6, and 12 months postoperatively, and then annually. The circumstances of many of our patients made traveling for follow-up evaluation difficult, despite our provision of satellite clinics in strategic regions of Uganda. Our social work staff was instrumental in finding many patients during home visits throughout the country who might have otherwise been lost to follow-up. Provision was often made for such patients to travel to the clinic for evaluation.

A good outcome was determined using the same parameters as those for adequate shunt function: deceleration of head growth, decompression of the anterior fontanel, and stabilization or decrease in ventricular size as determined on ultrasonography or CT images.

Statistical analysis was performed using SPSS Version 14.0 (SPSS Inc.). Survival analysis was performed using Kaplan–Meier techniques to analyze the population both by intent-to-treat analysis (all patients proceeding to the operating room to undergo an ETV-CPC) and those who had at least 1 ETV-CPC procedure completed. These groups were analyzed for progression-free survival (time to failure) and shunt-free survival. For the former outcome variable, ETV-CPC failures were defined as patients who died either within 30 days of surgery or from other disease or patients who returned to the operating room for another procedure. Patients who died from causes clearly not related to surgery or their disease (such as from malaria) and patients lost to follow-up were censored at the time of the last follow-up visit. For shunt-free survival, failures were defined as patients who died either within 30 days of surgery or from their disease or patients who required placement of a shunt. To explore factors that predicted failure of the ETV-CPC procedure, we performed a multivariate logistic regression to evaluate scarring of the CP, scarring of the cisterns, patency of the aqueduct, age of the patient at time of surgery, and visualized flow across the ETV as potential explanatory variables.

Results

Incidence of Hydrocephalus in the Population With Myelomeningocele

Between January 2001 and June 2006 338 infants were treated, in whom a myelomeningocele was repaired prior to 6 months of age. Of this group, 169 required treatment for hydrocephalus (including 115 consecutive patients who proceeded to surgery with the intention to undergo treatment using the ETV-CPC procedure), and 89 were followed-up for a minimum of 6 months who did not require treatment for hydrocephalus. An additional 64 children who did not require treatment for hydrocephalus were lost to follow-up before 6 months after repair of the myelomeningocele, 14 additional patients were not treated but died within 1 month of myelomeningocele closure, and 2 were not treated who died between 1 and 6 months after closure. Therefore, of 258 patients with >6 months of follow-up, 66% required treatment for hydrocephalus. If it were assumed that all patients who died or were lost to follow-up before 6 months (an additional 80 patients) would have developed hydrocephalus, then a maximum of 74% of the group would have required treatment. Making the converse assumption, that none of those patients lost to follow-up before 6 months developed hydrocephalus, places the minimum incidence of hydrocephalus in our spina bifida population at 50%.

Results of ETV-CPC as the Primary Treatment

Between February 2003 and June 2006, 115 consecutive infants with hydrocephalus in association with myelomeningocele proceeded to surgery with the intention of...
undergoing an ETV-CPC procedure. Of these 115 patients, 4 underwent ETV alone because the CP was completely obliterated by scarring from prior ventriculitis. Nine patients underwent VPS or reservoir placement because of congenital or postinflammatory anatomical distortion or poor visibility. The reasons for abandoning the ETV are summarized in Table 1. Eight patients were lost to follow-up before 1 month, and 1 patient died within 1 month of the operation. This 1 patient classified as experiencing operative death (defined as death from any cause within 30 days of surgery) in the group did well during the procedure and the immediate postoperative period, but died at home on postoperative Day 9, 2 days after discharge, of an unknown cause. Thus, 93 patients with > 1-month follow-up underwent ETV-CPC as the primary treatment for their hydrocephalus.

The mean age of the patients at the time of operation was 3.0 months and the median age was 2.0 months. All infants were < 1 year of age, with the exception of 1 child aged 15 months, at the time of initial treatment for hydrocephalus. The mean and median age at the time of treatment for patients with successful outcomes was 3.3 and 2.0 months, respectively. The mean and median age at time of treatment for those in whom ETV-CPC failed was 2.0 months. Among 8 infants presenting for myelomeningocele closure within a few days of birth, ETV-CPC was performed prior to 1 month of age at 1–2 weeks after closure (mean 1.5 weeks following closure of the myelomeningocele). Of these 8 patients, 7 had successful outcomes with a mean follow-up of 19.9 months (range 1–44 months).

Of the 93 patients, 71 (76%) had good outcomes with no need for further surgery. Both the mean and median follow-up time was 19.0 months (range 1–49 months), with 75 patients (81%) followed up for 6 months or more. The mean and median time to treatment failure was 3.3 and 2.4 months, respectively (range 2 weeks–10 months). Of the 22 treatment failures, 19 (86%) failed within 6 months, with only 3 patients treated for ETV-CPC failure > 6 months later; 14 treatments (64%) failed within 3 months of the operation. Life table analysis is demonstrated in Fig. 2. In an intent-to-treat model, including patients in whom ETV-CPC was not performed for technical reasons, a Kaplan–Meier analysis suggested that 67% of patients would be successfully treated using a single ETV-CPC procedure. In this same population, 78% of patients would remain without a shunt in the long term by using the strategy of performing a repeat ETV after the first treatment failure if the stoma had closed.

There was 1 operative death (1.1%). Among the 71 patients followed up who had good outcomes, 8 were known to have died later (1–6 months after surgery), thus terminating further follow-up. None of the deaths were known to be related to hydrocephalus or its treatment. Three patients died of malaria, measles, and a gastrointestinal illness, respectively. The cause of death in the other patients was not known. There was no indication that any of the deaths were related to treatment failure. These patients were censored at the time of the last follow-up in the life table analysis.

**Predictors of Treatment Failure**

Patient age at the time of surgery, scarring of the interpeduncular and/or preponsine cisterns and of the CP, evidence for CSF flow across the ETV stoma as noted and recorded at the time of surgery, and whether the ostium of the aqueduct was open or closed were all recorded for later evaluation as possible predictors of outcome. Among the 93 patients, the status of the cistern was reported at the time of surgery in 74, and a description of CSF flow across the stoma was reported in 91. Of 11 patients with scarred cisterns, 6 (55%) had successful outcomes, whereas 50 (79%) of 63 with unscarred cisterns had successful outcomes. Poor or no CSF flow was only reported in 3 of 22 treatment failures (the remaining 19 showed good evidence of flow), and in none of those with a good outcome. Whether there was scarring of the CP was recorded in 66 patients. Of 58 patients without scarring, 45 (78%) had successful outcomes, and of the 8 with CP scarring, 3 (38%) had a good outcome. The appearance of the aqueduct at surgery was recorded in 84 patients. In 59 (78%) of 76 with open aqueducts and in 6 (75%) of 8 with closed aqueducts, the outcome of the ETV-CPC procedure was good. A multivariate logistic regression analysis was performed and revealed that scarring of the CP (p = 0.026) and scarring of the cisterns (p = 0.021) were statistically related to a higher rate of treatment failure. On the other hand, age at the time of surgery, poor flow through the ETV, and the status of the aqueduct were not predictive of treatment failure.

**Management of Treatment Failure**

In general, those patients who experienced early treatment failure underwent shunt placement, whereas those in whom the ETV-CPC initially appeared to be successful were selected for repeat endoscopy. Fifteen of the 22 patients who experienced treatment failure underwent simple shunt placement, with a mean time to presentation of 2.1 months (range 0.5–4 months). The remaining 7 patients, with a mean time to failure of 5.9 months (range 1.75–10 months), underwent repeat ventriculostomy with the intent to reopen a closed ETV.

The findings in the 7 patients who underwent repeat ventriculostomy for treatment failure are detailed in Table 2. In 6 of these patients, the ETV was obstructed and was able to be reopened, whereas in 1 patient the ETV

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**TABLE 1**

<table>
<thead>
<tr>
<th>Reason for abandoning the ETV attempt (technical failures)</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>postinflammatory distortion of intraventricular anatomy</td>
<td>4</td>
</tr>
<tr>
<td>thick 3rd ventricle floor/absence of landmarks</td>
<td>2</td>
</tr>
<tr>
<td>cisterns obstructed by scar</td>
<td>1</td>
</tr>
<tr>
<td>bilateral absence of foramina of Monro</td>
<td>1</td>
</tr>
<tr>
<td>cloudy CSF/poor visibility</td>
<td>1</td>
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was open into a clean cistern, and therefore a VPS was placed. It is significant that in every case the previously cauterized CP was found to have been mostly replaced by a thin white line of scar tissue, with only a few “sprouts” of residual CP remaining to be cauterized. Thus, after a mean interval of nearly 6 months, regeneration of the CP was not observed to have occurred to a significant degree. Among the 6 patients in whom an obstructed ETV was reopened, 4 had good outcomes with a mean follow-up duration of 16.1 months (range 5–27 months). Therefore, of 93 patients, 75 (81%) remained shunt-independent. This result is represented as shunt-free survival in the Kaplan–Meier curves of Fig. 2.

Discussion

Treating hydrocephalus in infants is particularly challenging in less developed countries because of the inherent obstacles in managing shunt malfunction. The shunt-dependent child whose fontanels have closed is at risk for serious morbidity or death from shunt malfunction if there is no urgent access to appropriate treatment. Given the ongoing lifetime risk and high probability of at least 1 shunt malfunction, an alternative treatment for hydrocephalus that offers a reasonable chance of avoiding shunt-dependence is very desirable in this context if the successes are durable. In other words, this alternative treatment is to be preferred if—unlike shunts—there does not tend to be a steady rate of failure after the early period of postoperative monitoring.

This is the largest study of primary endoscopic management of hydrocephalus in infants with myelomeningocele. Teo and Jones10 reported on a retrospective study of 69 patients with myelomeningocele ranging from 1 week to 32 years in age in whom ETV was performed over a 17-year period. Use of an ETV alone was the initial treatment in only 14 patients, and in the remaining patients ETV provided an alternative to shunt revision. The overall success rate in this study was 72%, but among 8 infants younger than 6 months of age it was 12.5%, and among 19 children younger than 2 years of age it was 53%. Of the 14 patients in whom ETV was used as the primary treatment, shunt dependence was successfully avoided in only 4 (29%).

The ETV-CPC procedure has been shown to be more successful than ETV alone in infants younger than 1 year of age.13 A plausible explanation for the added benefit of CPC is that it reduces CSF production sufficiently to compensate for a “communicating” component of the hydrocephalus that may exist in infants who do not have sufficiently developed CSF circulation and absorption capacity to accommodate the new efflux of CSF through the ETV stoma. This lack of capacity may be a consequence of the incompletely developed status of the arachnoid granulations in newborns as suggested by Oi and Di Rocco.6 In other words, the combined procedure may si-
Results of ETV-CPC in African infants with myelomeningocele

multaneously address the obstructive component among patients who would experience failure with CPC alone, and the communicating component among those who would experience failure with ETV alone; the combined technique would thus result in a greater success rate than either procedure alone. Alternative hypotheses may apply if paradigms other than the bulk flow theory of hydrocephalus are assumed, as suggested most recently by Greitz and Madsen et al. Whatever the mechanism is, the effectiveness of combining the 2 procedures was most evident among infants with spina bifida.

Performing ETV in patients with myelomeningocele is technically more challenging because of the anatomical variations described above, and familiarity with these anomalies is required. Furthermore, using the flexible endoscope to cauterize the CP in both lateral ventricles from a single approach, including CP in the temporal horns, is a distinct endoscopic skill, but it can be readily mastered with practice. That these skills are readily transferable is supported by the senior author’s experience to date in training 8 surgeons in 6 developing countries to become competent in the ETV-CPC technique despite their absence of previous ventriculoscopy experience. Figure 3 demonstrates preoperative and 5-month postoperative midaxial CT scans in an infant with myelomeningocele, in whom ETV-CPC was performed independently at CURE Children’s Hospital of Uganda by a former trainee of the senior author. Note the decrease in ventricular volume as well as the absence of the CP in the left atrium (contralateral to the surgical entry point) in comparison with the preoperative study.

In this paper we follow up on the results of this technique in a larger number of infants with spina bifida who have now been followed up for a longer duration, and it is notable that the rate of success (76%) is unchanged from the initial report. Although we chose standard clinical criteria for treatment failure typical of those used to assess treatment by shunt placement, bias cannot be excluded because this was not a blinded study. The life table analysis of Fig. 2 suggests that using ETV-CPC as the primary treatment for hydrocephalus in infants with myelomeningocele should enable one to avoid another hydrocephalus-related operation in 72%, and that with reopening obstructed ETVs in those who experience treatment failure, shunt-dependency would be avoided in 78% (Fig. 2D). Furthermore, these data suggest that most treatment failures occur early and are rare after 6 months, suggesting a substantially lower long-term failure rate than has been reported for shunt placements in this population.

Drake and colleagues have highlighted the occurrence of “late rapid deterioration” in patients who previously had undergone successful ETV. In that report, 16 cases were assembled from a review of the literature and an international survey. Of the 16 cases, 7 treatment failures occurred < 12 months after the operation, with 5 treatment failures in the first 6 months and 2 failures in the first 2 months. Thus, instances of treatment failure and rapid deterioration occurring more than a year after ETV appear to be truly uncommon. Nonetheless, it is important for patients, families, and healthcare providers to be aware of this rare possibility.

Unsuccessful outcomes presenting beyond the initial weeks of treatment likely occur from ETV closure or scarring in the cistern below a patent ETV, and earlier failures are assumed to occur largely from an inadequately treated communicating hydrocephalus, with insufficient subarachnoid circulation (from extraventricular obstruction) or CSF absorption. It appears that either mode of failure usually presents itself within the first 6 months of treatment. Furthermore, of those treatment failures that occurred from ETV closure, ETV reopening was successful in maintaining shunt-independence in about two-thirds of the cases with a mean follow-up > 16 months. This rate increased the overall shunt-free survival rate to ~ 80%.

The incidence of hydrocephalus in our population with spina bifida (66%, with a possible range of 50–74%) is less than that reported by other investigators. This lower incidence rate may reflect a greater reservation on our part to pursue treatment unless persistently progressive hydrocephalus was clearly evident, having observed that initially accelerated head growth and mild to modest ventriculomegaly sometimes stabilize over the first 1–2 months without intervention. This treatment philosophy, along with a mean patient age of 3 months at treatment, argues against a concern that treating infants in whom hydrocephalus would have arrested spontaneously falsely magnified the success of the ETV-CPC technique.

Conclusions

The ultimate goal of any hydrocephalus treatment is a normally developed brain in the patient. It is not currently known whether any one treatment is superior to another in this regard. An argument can be made, however, that unless shunt-dependence was clearly shown to have long-term cognitive advantages, a technique that successfully treats hydrocephalus by all clinical criteria while avoiding shunt-dependence (and treating it with less chance of a second operation) is to be recommended for patients in less developed countries whenever possible. This study suggests that primary treatment of hydrocephalus in infants.
with myelomeningocele using ETV-CPC may be expected to avoid shunt-dependence in 3 of every 4 patients treated, with a lower infection rate and less chance of the need for additional operations. In this group, evidence of prior infection as evidenced by scarring of the cisterns or CP was associated with treatment failure, whereas younger age was not.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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