Long-term outcome for endoscopic third ventriculostomy alone or in combination with choroid plexus cauterization for congenital aqueductal stenosis in African infants

Clinical article

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Object. The authors have previously reported on the overall improved efficacy of endoscopic third ventriculostomy (ETV) combined with choroid plexus cauterization (CPC) for infants younger than 1 year of age. In the present study they specifically examined the long-term efficacy of ETV with or without CPC in 35 infants with congenital aqueductal stenosis treated at CURE Children's Hospital of Uganda during the years 2001–2006.

Methods. Infants with congenital aqueductal stenosis were treated during 2 distinct treatment epochs: all underwent ETV alone, and subsequently all underwent ETV-CPC. Prospectively collected data in the clinical database were reviewed for all infants with an age < 1 year who had been treated for hydrocephalus due to congenital aqueductal stenosis. Study exclusion criteria included: 1) a history or findings on imaging or at the time of ventriculoscopy that suggested a possible infectious cause of the hydrocephalus, including scarred choroid plexus; 2) an open aqueduct or an aqueduct obstructed by a membrane or cyst rather than by stenosis; 3) severe malformations of the cerebral hemispheres including hydranencephaly, significant segments of undeveloped brain, or schizencephaly; 4) myelomeningocele, encephalocele, Dandy-Walker complex, or tumor; or 5) previous shunt insertion. The time to treatment failure was analyzed using the Kaplan-Meier method to construct survival curves. Log-rank (Mantel-Cox) and Gehan-Breslow-Wilcoxon tests were used to determine whether differences between the 2 treatment groups were significant.

Results. Thirty-five patients met the study criteria. Endoscopic third ventriculostomy alone was performed in 12 patients (mean age 4.7 months), and combined ETV-CPC was performed in 23 patients (mean age 3.5 months). For patients without treatment failure, the mean and median follow-ups were, respectively, 51.6 and 48.0 months in the ETV group and 31.2 and 26.4 months in the ETV-CPC group. Treatment was successful in 48.6% of the patients who underwent ETV alone, as accurately predicted by the Endoscopic Third Ventriculostomy Success Score (ETVSS), and in 81.9% of the patients who underwent ETV-CPC (p = 0.0119, log-rank test; p = 0.0041, Gehan-Breslow-Wilcoxon test; HR 6.42 [95% CI 1.51–27.36]).

Conclusions. Combined ETV-CPC is significantly superior to ETV alone for infants younger than 1 year of age with congenital aqueductal stenosis. The fact that the outcome for ETV alone was accurately predicted by the ETVSS suggests that these results are applicable in developed countries.

Key Words • endoscopic third ventriculostomy • hydrocephalus • choroid plexus cauterization • congenital aqueductal stenosis • Africa • Endoscopic Third Ventriculostomy Success Score

Rural East Africa presents significant roadblocks to the timely maintenance of ventriculoperitoneal shunt function. Thus, the condition of shunt dependence is intuitively more dangerous in this context.

Abbreviations used in this paper: CCHU = CURE Children's Hospital of Uganda; CPC = choroid plexus cauterization; ETV = endoscopic third ventriculostomy; ETVSS = ETV Success Score.
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alocele, and Dandy-Walker complex.9–11,15 In the present study we examined the efficacy of ETV-CPC in infants with congenital aqueduct stenosis.

Methods

After June of 2001 all infants presenting to CCHU for the treatment of hydrocephalus underwent primary ventriculoscopy, initially for attempted ETV9 and subsequently for attempted combined ETV-CPC.7,8 Thus, although the study was not a randomized prospective trial, treatment was determined by the epoch of treatment and did not involve patient selection. Our technique for the combined ETV-CPC procedure has been described in detail elsewhere, as have the operative morbidity and mortality rates.7 The CPC portion of the procedure utilized a 3.7-mm flexible fiberoptic ventriculoscope and a Bugby wire at the lowest effective monopolar current to cauterize the plexus from the foramen of Monro to the temporal horn in both lateral ventricles. This is accomplished through a single right frontal approach at the time of the ETV. Data on all patients were prospectively recorded in a clinical database. This study includes some patients previously reported on in 2005 and extends their follow-up.7

With institutional approval, the CCHU clinical database was searched to identify all infants younger than 1 year of age in whom an ETV or ETV-CPC had been performed for the treatment of hydrocephalus whose etiology was congenital aqueductal stenosis or occlusion between 2001 and 2006 (the time during which the senior author [B.C.W.] was the primary surgeon). Although we were able to reliably predict aqueductal obstruction from the appearance of the fourth ventricle on ultrasonography or CT,8 it was confirmed by direct endoscopic inspection of the aqueduct. Only patients with a history, imaging studies, and intraoperative findings consistent with congenital hydrocephalus whose apparent cause was congenital aqueductal stenosis or occlusion were included in the 2 study cohorts. One patient in whom ETV and only partial CPC had been performed was excluded. One patient in each treatment group underwent ETV via the lamina terminalis rather than the third ventricular floor. Patients with any of the following features were excluded from analysis: 1) history or findings on imaging or at the time of ventriculoscopy that suggested a possible infectious cause of the hydrocephalus, including scarred choroid plexus; 2) an open aqueduct or an aqueduct obstructed by a membrane or cyst rather than stenosis; 3) severe malformations of the cerebral hemispheres including hydranencephaly, significant segments of undeveloped brain, or schizencephaly; 4) myelomeningocele, encephalocele, Dandy-Walker complex, or tumor; or 5) previous shunt insertion. Prior to 2002, infants underwent cranial ultrasonography for preoperative and postoperative analysis, but thereafter CT scanning was used. Patients were followed up in our outpatient clinic, and efforts were made to update the status of those who had been lost to follow-up. In 3 patients (2 ETV and 1 ETV-CPC) the latest follow-up occurred by telephone interview to ensure that the child was still alive and well with no signs or symptoms of untreated hydrocephalus. In 5 patients (3 ETV and 2 ETV-CPC) the latest follow-up occurred via home visit, but all other patients were assessed in our clinic by a CCHU physician. Home visits for 7 patients revealed that the children were deceased, and the date and circumstances of death were gathered from the family.

We used standard treatment success criteria: a shift in head circumference growth to a normal or less-than-normal rate, as plotted on a standard growth chart; decompression of the anterior fontanel; relief from symptoms of elevated intracranial pressure (such as irritability and vomiting); resolution of abnormal eye findings (for example, sunsetting or sixth cranial nerve palsy); and a decrease or arrest in ventriculomegaly, as determined on ultrasonography or CT scanning by using the Evans ratio or frontooccipital horn ratio, respectively. Treatment failure was defined as repeat surgery for hydrocephalus (repeat endoscopy or shunt placement).

We analyzed the time to treatment failure using the Kaplan-Meier method to construct survival curves. Log-rank (Mantel-Cox) and Gehan-Breslow-Wilcoxon tests were used to determine whether differences between the 2 groups were significant. All analyses were performed using GraphPad Prism 5.01 (GraphPad Software, Inc.).

Results

Thirty-five patients met the study criteria, including 19 males (9 ETV and 10 ETV-CPC) and 16 females (3 ETV and 13 ETV-CPC). Endoscopic third ventriculostomy alone was performed in 12 infants at a mean age of 4.7 months (median 4.9 months). Combined ETV-CPC was performed in 23 infants at a mean age of 3.5 months (median 3.1 months). For patients without treatment failure, the mean and median follow-ups were, respectively, 51.6 and 48.0 months in the ETV group and 31.2 and 26.4 months in the ETV-CPC group. The longer follow-up for the ETV group is expected, since this represents the first treatment epoch. All reoperations for treatment failure occurred between 0.46 and 6.21 months after the initial operation. The mean and median times to reoperation for treatment failure were, respectively, 1.72 and 1.55 months in the ETV group and 4.00 and 4.73 months in the ETV-CPC group.

The survival curves in Fig. 1 demonstrate the time to treatment failure for the 2 patient groups. Among those treated with ETV alone, the procedure was successful in 48.6% , as compared with 81.9% of those treated using combined ETV-CPC. The difference was statistically significant as determined by the log-rank test (p = 0.0119) and the Gehan-Breslow-Wilcoxon test (p = 0.0041). The hazard ratio was 6.42 (95% CI 1.51–27.36).

Discussion

Age is an important determinant of outcome for ETV.3,15 Because the higher failure rate of ETV among infants may result from a residual component of “communicating” hydrocephalus in some children because of an age-related inefficiency in CSF absorption, we surmised that reduction of the choroid plexus might improve the outcome of ETV in this young age group. We subsequently demonstrated an overall significant improvement
in outcome for the combined procedure among infants younger than 1 year of age, although the difference lacked statistical significance for the subset with nonpostinfectious hydrocephalus that had aqueduct obstruction.7 The present study extends this work to a larger number of patients in this subset with longer follow-ups and the utilization of survival analysis. It also utilizes tighter restrictions for inclusion criteria to evaluate the more homogeneous population of patients with congenital aqueduct stenosis and to better ensure similarity between treatment groups. Patients with any other recognizable severe brain malformation, evidence of tumor or infection, or any other causes of aqueduct obstruction, such as webs or cysts seen on endoscopy, were excluded from analysis. The stringent exclusion criteria used suggest similarity between treatment groups as regards hydrocephalus etiology. Note that the ETV group had relatively fewer girls and that the ETV-CPC group was somewhat younger at the time of treatment.

Survival analysis demonstrated a significantly better outcome for combined ETV-CPC (81.9%) than for ETV alone (48.6%) as treatment for hydrocephalus due to congenital aqueduct stenosis among infants younger than 1 year of age (p = 0.0119, log-rank test; p = 0.0041, Gehan-Breslow-Wilcoxon test; HR 6.42 [95% CI 1.51–27.36]). All known failures occurred by 6.2 months. Combined ETV-CPC appears to offer an excellent alternative to primary shunt placement in this young age group, one with less chance of a second operation for hydrocephalus as compared with either ventriculoperitoneal shunt placement or ETV alone. As we have argued elsewhere, this is especially important in the context of limited resource environments in which the maintenance of shunt function is problematic.7,8

It is unknown whether there is any difference in developmental outcome between those with successful endoscopic treatment and those treated with shunt placement. For infants with hydrocephalus associated with myelomeningocele, we were unable to demonstrate a significant difference.14 The ongoing International Infant Hydrocephalus Study promises to provide a rigorous answer to this question for infants with congenital aqueduct stenosis.6 Kulkarni and coauthors3 described an ETV outcome prediction score (the ETVSS) using the parameters of patient age, etiology of hydrocephalus, and previous shunt placement. The ETVSS was based on patient data from developed countries and has recently been shown to be valid when applied retrospectively to patient groups treated at other institutions in developed countries.13 Similarly applying the ETVSS to patients in the present study (respective mean and median ages of 4.2 and 3.8 months, etiology of aqueductal stenosis, and no prior shunt) predicts success in 50%, which coincides with our observed success in 48.6% of those treated via ETV alone, while significantly underestimating the 81.9% success rate for those who underwent ETV in combination with CPC. We have described a different ETV scoring system based on our initial experience with attempted ETV or ETV-CPC in more than 1400 patients in Uganda and found that the ETVSS was poorly predictive of success in the Ugandan cohort.13 The parameters for this score were patient age, etiology of hydrocephalus (myelomeningocele, postinfectious, or other), and degree of CPC (none, partial, or complete bilateral). When this Uganda-based score is applied to patients in the current study, the predicted likelihood for success of the combined ETV-CPC procedure is about 65%, still less than the 81.9% we report here despite accounting for the CPC. Moreover, applying the same score to those who underwent ETV alone predicts only around 30% success as compared with the actual 48.6%, also an underestimate. The Uganda-based score was determined from a population in which congenital aqueduct stenosis was a distinct minority and was lumped in with all other causes of hydrocephalus (aside from infection and myelomeningocele), without accounting for the status of the aqueduct. We subsequently demonstrated the independent effects of aqueduct patency, as well as the status of the prepontine cistern, on outcome.12 Given that we evaluated congenital aqueduct stenosis as a distinct subset in the present study, it is not surprising that the ETVSS, which is based on a developed world population, predicts a result for ETV alone that is nearly identical to what we report for the African population here, because there should be no intrinsic difference in outcomes for the same etiology of hydrocephalus and age of treatment in the 2 populations. We have previously reported that differences in ETV outcomes between children in developed countries and those in sub-Saharan Africa can be fully accounted for by disparities of etiology and the addition of CPC.13 The fact that the ETVSS so accurately predicted the success of ETV in congenital aqueduct stenosis for our practice in Uganda supports the relevancy of our other outcome data for distinct etiologies of hydrocephalus (myelomeningocele, encephalocele, and Dandy-Walker complex) to neurosurgical practices in the developed world.9,11,15

The limitations of this study must be recognized. It was hampered by the lack of MRI studies at CCHU. There is the potential for more patient heterogeneity if some abnormalities accompanying the aqueductal stenosis were undetected, such as tectal glioma, callosal dysgenesis, or neuronal migrational anomalies. However,
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the significance of such variations for the conclusions of the study are likely negligible. Another limitation is the extent of follow-up. For patients without treatment failure the mean and median follow-up were, respectively, 51.6 and 48.0 months in the ETV group and 31.2 and 26.4 months in the ETV-CPC group; however, 7 patients had <6 months of follow-up. We used the standard Kaplan-Meier method to adjust for patients lost to follow-up. In addition, the mean and median times to reoperation for treatment failure were, respectively, 1.72 and 1.55 months in the ETV group and 4.00 and 4.73 months in the ETV-CPC group, with a maximum time to reoperation of 6.2 months. Most ETV failures occur early, with a steep rate of failure in the first 3–6 months accounting for the majority of cases. Of course, later failures can occur, and thus in either group, treatment failure beyond the time of follow-up is possible.

Conclusions

Combined ETV-CPC is significantly superior to ETV alone in infants younger than 1 year of age with hydrocephalus from congenital aqueductal stenosis, with success in 81.9% of patients. The fact that our outcome for ETV alone was accurately predicted by the ETVS suggests that our results are broadly applicable to all infants with this specific diagnosis.

Disclosure

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

Author contributions to the study and manuscript preparation include the following. Conception and design: Warf. Acquisition of data: all authors. Analysis and interpretation of data: Warf. Drafting the article: Warf. 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: Warf. Statistical analysis: Warf. Administrative/technical/material support: all authors. Study supervision: Warf.

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