Treatment of cerebrospinal fluid shunt infections in children using systemic and intraventricular antibiotic therapy in combination with externalization of the ventricular catheter: efficacy in 34 consecutively treated infections

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Object. There are no randomized studies comparing the efficacy of different antibiotic regimens for the treatment of cerebrospinal fluid (CSF) shunt infections, and in the studies that have been reported, efficacy data are limited. The aim of this study was therefore to report the authors’ experience using a specific protocol for the management of shunt infections in children. Standard treatment included a two-stage procedure involving externalization of the ventricular catheter in combination with intraventricular and systemic administration of antibiotic medication followed by shunt replacement. Intraventricular treatment consisted of daily instillations of vancomycin or gentamicin with trough concentrations held at high levels of 7 to 17 mg/L for both antibiotic agents.

Methods. During a 13-year study period, the authors treated 34 consecutive intraventricular shunt infections in 30 children. Infections with coagulase-negative staphylococci predominated, and Gram-negative bacterial infection occurred in five children. Ten of the children were initially treated with intravenous antibiotic therapy for at least 3 days, but this treatment did not sterilize the CSF. After externalization of the ventricular catheter, high-dose intraventricular treatment was given for a median of 8 days (range 3–17 days) before shunt replacement.

Results. The CSF was found to be sterile (cultures were negative for bacteria) in one of three, seven of eight, 20 of 20, and six of six cases after 1, 2, 3, and more than 3 days’ treatment, respectively. In no case was any subsequent culture positive after a negative result had been obtained. Clinical symptoms resolved in parallel with the sterilization of the CSF. There were no relapses or deaths during the 6-month follow-up period, and there have been none as of April 2007.

Conclusions. Despite the ventricular catheter being left in place and the short duration of therapy, the treatment regimen described by the authors resulted in quick sterilization of the CSF, a low relapse rate, and survival of all patients in this series. (DOI: 10.3171/PED-07/09/213)

KEY WORDS • antibiotic treatment • cerebrospinal fluid • intraventricular antibiotic instillation • pediatric neurosurgery • shunt infection

CEREBROSPINAL Fluid shunt infections are among the most common infections faced by pediatric neurosurgeons, with incidence rates ranging from 8 to 12% reported in modern studies.¹⁶,¹⁷ Despite the frequency with which these infections are encountered, management strategies vary significantly among pediatric surgeons.¹⁶,¹²,²³ The options for treatment have been 1) a two-stage procedure involving removal of the entire shunt, placement of an EVD, and shunt replacement after sterilization in combination with antibiotic treatment and 2) a one-stage procedure involving removal of the shunt and immediate replacement with a new shunt in combination with antibiotic therapy or antibiotic treatment alone. The efficacy of these treatment strategies has been evaluated in several studies, but thus far there has been only one small randomized trial—that of James et al.,¹¹ who demonstrated that the combination of shunt component removal and antibiotic therapy was superior to treatment with antibiotics alone. In an analysis of the results of 18 studies in which authors reported the results of the two-stage procedure, the one-stage procedure, or antibiotic treatment alone, cure rates were found to be 96, 65, and 34%, respectively.²⁴ In a recent assessment of the three approaches, approximately the same results were obtained.¹⁹

In the studies just discussed the antibiotic treatment was administered via the systemic or intraventricular route or both. Regarding evaluation of different antibiotic regimens, data are even more limited. There are no randomized trials, and as the effect is dependent on the surgical management, it is difficult to compare and assess the efficacy of different

Abbreviations used in this paper: CI = confidence interval; CSF = cerebrospinal fluid; EVD = external ventricular drain.
antibiotic treatments without standardizing the surgical procedure. The selection of antibiotic agents and the duration of antibiotic treatment have therefore been determined on the basis of susceptibility patterns of causative agents; information regarding the medication's penetration into the CSF compartment; results from open, nonrandomized studies; and personal experience, all of which have led to many different treatment regimens.6,19,23

Several years ago a high efficacy of intraventricular administration of vancomycin together with systemic antibiotic medication for the treatment of staphylococcal shunt infection was demonstrated by Bayston et al.3 and Swayne et al.20 On the basis of the results of these studies and the studies by James et al.11 and Yoge24 as well as the belief that intraventricular administration leading to a high bactericidal concentration is of benefit in these cases, an institutional protocol for the treatment of shunt infection in children was developed at the Department of Pediatric Surgery at our hospital. This protocol included a two-stage procedure in combination with an initial antibiotic treatment composed of high-dose intraventricular antibiotic therapy in addition to intravenously or orally administered antibiotic medication. Based on our own previous experience and the expected effect of the antibiotic treatment, we externalized the ventricular catheter instead of placing a whole EVD.

The aim of the present study is to assess the efficacy of this treatment regimen with respect to cure, relapse, and mortality rates.

**Clinical Material and Methods**

The medical records of all children with hydrocephalus operated on by a pediatric surgeon at the Departments of Pediatric Surgery or Neurosurgery, University Hospital, in Uppsala, during a 13-year period (January 1992–December 2004) were reviewed to identify cases involving shunt infection.

In children with suspected infection, externalization was performed proximal to the valve, and the distal catheter tip was sent for culturing. The suspicion of infection was mild in some cases, and therefore in those patients only the distal catheter was initially externalized at the thoracic level. If an intraventricular infection was subsequently verified, the distal catheter and the valve were removed and externalization proximal to the valve was carried out. Samples of CSF were obtained from the externalized catheter for culture, analysis of glucose content, and determination of numbers of leukocytes. The CSF cultures were observed for a minimum of 7 days. In addition, blood glucose levels, white blood cell counts, and serum C-reactive protein levels were determined.

For the diagnosis of shunt infection, the criteria used in this study were modified slightly from those employed in a recent study by Wang et al.25 Intraventricular shunt infection was defined as 1) growth of bacteria from the catheter tip or CSF and 2) the presence of a glucose ratio (CSF/blood) of less than 0.45, a CSF glucose concentration less than 2.5 mmol/L, or a CSF leukocyte count of more than 250 × 10⁶ cells/L. In some cases the CSF glucose concentration was not available. If the leukocyte count in these cases did not meet the criteria for intraventricular shunt infection, the infection was classified as suspected. Cure was defined as sterilization of CSF and resolution of clinical symptoms. Relapse was defined as infection with the same causative agent within 6 months after shunt replacement and withdrawal of antibiotic treatment.

The patient’s age at onset of infection, clinical presentation, treatment, treatment outcome in the form of sterilization of cultures, data regarding relapse and/or death, as well as the pathogenesis of hydrocephalus and the causative agent of the infection were recorded in cases of shunt infection.

In addition to externalization of the ventricular catheter, standard treatment of proven intraventricular infections included daily intraventricular antibiotic instillations. The dosage depended on the estimated size of the ventricular system and the results of CSF antibiotic concentration analyses. After intraventricular antibiotic administration, the ventricular drainage tube was clamped for 1 hour. A CSF sample was obtained for antibiotic concentration analysis just before the next instillation. The aim was to maintain a concentration between 7 and 17 mg/L for both vancomycin and gentamicin. These concentrations were chosen as being well above the minimal inhibitory concentrations of sensitive bacteria. Cerebrospinal fluid cultures were to be obtained 2 or at the latest 3 days after initiation of intraventricular treatment. If positive for bacteria, cultures were to be repeated daily until negative results were obtained. Depending on culture results, CSF laboratory parameters, and the patient’s clinical condition, intraventricular antibiotic therapy was to be continued for 5 to 10 days until shunt replacement. At shunt replacement the same bur hole was used, but the ventricular catheter was exchanged and a new location was used for the shunt and the distal catheter. Systemic antibiotic treatment was concomitantly given up to the day of shunt replacement, whereupon it was withdrawn. On the first 2 or 3 days and on the day of shunt replacement, antibiotic medications were to be administered intravenously. On the other days, antibiotic agents could be administered either orally or intravenously at the discretion of the physician responsible for the case and according to the clinical condition of the patient. For various reasons, such as initiation of treatment at departments other than the Department of Pediatric Surgery or no surgical specialist in the management of shunt infection being available, the protocol was not accurately followed in all cases. Therefore, in 10 children, preliminary therapy consisting solely of the intravenous administration of antibiotic medication was undertaken before the start of intraventricular treatment.

In four children treated with intravenous antibiotic therapy alone, CSF was collected for antibiotic concentration analysis at 2 hours after the intravenous injection of meropenem, cefotaxime, and cloxacillin and at 1 hour after the end of the 2-hour infusion of vancomycin. Vancomycin and gentamicin CSF concentrations were analyzed by fluorescence polarization immunoassay (TDX Flex, Abbott Diagnostics), and meropenem, cefotaxime, and cloxacillin concentrations were analyzed by microbiological methods.

The exact confidence limits for binomial distribution were calculated in the statistical determination of the 95% CI for cure rate, relapse rate, and mortality rate.5

**Results**

During the study period, 474 shunt operations were performed in 237 children ranging in age from 0 to 15 years.
Intraventricular antibiotic administration in shunt infections

There were 30 verified and four suspected consecutive shunt infections in 30 children. One child had three and two children two separate shunt infections with different bacteria. In all cases, bacterial growth was evident in cultures of specimens from both the catheter tip and CSF. Only 32 shunt placement procedures were performed after antibiotic treatment because two of the children with arachnoid cysts were considered not shunt dependent after their infections were successfully treated.

The cause of hydrocephalus was myelomeningocele in 12 patients, hemorrhage in 10, aqueduct stenosis in five, and other reasons in three. Causative bacteria in relation to the patients’ age at infection are presented in Table 1, and clinical characteristics at admission are presented in Table 2.

Cure Rate

The effect of intravenous antibiotic treatment alone, with or without externalization of the shunt system, and the CSF antibiotic concentrations obtained during this initial treatment in four cases are summarized in Table 3. As shown in the table, all four children still had positive culture results after this initial therapy. In addition, six children treated for a median of 6 days (range 3–10 days) with intravenous antibiotics alone while the whole shunt system was left in place, pending externalization and start of intraventricular therapy, all demonstrated persisting positive CSF cultures.

After initiation of intraventricular antibiotic treatment and externalization of the ventricular catheter, all infections were cured (95% CI: 89.8 to > 99.99%). At the start of intraventricular antibiotic treatment, all cultures were positive, and when all follow-up culture results are considered together, sterilization with negative cultures was found in one of three, seven of eight, 20 of 20, and six of six patients after 1, 2, 3, and more than 3 days, respectively. In no case was any subsequent culture positive after a negative culture had been obtained. Clinical symptoms resolved before or in parallel with sterilization of the CSF. The intraventricular catheter was accidentally withdrawn in four children after 1, 2, 5, or 7 days of intraventricular treatment, and a new ventricular catheter was inserted on the same day in each case.

Specific Treatment and Cure Rate in Different Infections

Intraventricular shunt infections that were caused by coagulase-negative staphylococcal or *Staphylococcus aureus* were treated with daily intraventricular instillation of vancomycin and a few days of intravenous administration of vancomycin or cloxacillin, followed in some cases by oral administration of flucloxacinil. The intraventricular vancomycin dose varied between 1 and 10 mg per day. The first CSF cultures obtained after initiation of intraventricular treatment after two, three, and four or five instillations were all negative in three, 17, and four children, respectively. The coagulase-negative staphylococcal infection in one child was treated with externalization at the thoracic level and intravenous administration of vancomycin alone during 37 days with still-positive culture results before externalization of the ventricular catheter and initiation of intraventricular instillations. The first culture, which was obtained after two instillations, was negative. In another child, treatment of *S. aureus* infection was initiated with intravenously administered cloxacillin alone and externalization of the ventricular catheter. After 14 days with persisting positive cultures, intraventricular and intravenous therapy with vancomycin were started. The CSF culture was positive after 1 day, but the next culture, which was obtained after 3 days of treatment, was negative.

The patient with intraventricular *Propionibacter acne* infection was treated with vancomycin intraventricularly and intravenously. The first culture obtained after two instillations was negative. The enterococcal infection was treated with intravenously administered trimethoprim-sulphamethoxazole in addition to intraventricular vancomycin, and the CSF culture was negative after one instillation. The two *Escherichia coli* infections were treated with intraventricular gentamicin (1–4 mg) and intravenously administered trimethoprim-sulphamethoxazole in one case and cefuroxime in the other. The CSF cultures were negative at the first cultures obtained after three instillations in the former case and after six in the latter. The *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* infections were treated with systemic meropenem. In the case in which *P. aeruginosa* was identified, the child was treated with intraventricular gentamicin from the start; a positive culture was obtained after 2 days and a negative culture after 4 days of treatment. In the child with a *K. pneumoniae* infection, the catheter was initially externalized at the thoracic level and treatment according to the protocol was delayed 2 weeks resulting in persisting growth. After externalization proximal to the valve and initiation of intraventricular gentamicin therapy, the first CSF

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**TABLE 1**

*Causative bacteria in 30 patients stratified by patient age*  

<table>
<thead>
<tr>
<th>Causative Agent</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>11</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>5</td>
</tr>
<tr>
<td><em>P. acne</em></td>
<td>0</td>
</tr>
<tr>
<td>Enterococci</td>
<td>1</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>1</td>
</tr>
<tr>
<td>Other Gram-negative rods</td>
<td>3</td>
</tr>
<tr>
<td>β-hemolytic streptococci</td>
<td>0</td>
</tr>
</tbody>
</table>

* Some patients had more than one infection.

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**TABLE 2**

*Signs of shunt infection and laboratory parameters at admission*  

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median temperature in °C (range)</td>
<td>38.8 (37.0–40.9)</td>
</tr>
<tr>
<td>Redness over shunt system (no. of patients)</td>
<td>17</td>
</tr>
<tr>
<td>Median C-reactive protein level in mg/L (range)</td>
<td>123 (8–365)</td>
</tr>
<tr>
<td>Median blood WBC count x10⁹/L (range)</td>
<td>13.6 (5.9–41.6)</td>
</tr>
<tr>
<td>Median CSF WBC count x10⁹/L (range)</td>
<td>94 (0–5560)</td>
</tr>
<tr>
<td>Median glucose ratio (range)</td>
<td>0.16 (0.09–0.45)</td>
</tr>
<tr>
<td>Median glucose concentration in mmol/L (range)</td>
<td>0.5 (0.25–2.4)</td>
</tr>
</tbody>
</table>

* Data were available for 34 patients unless otherwise indicated. Abbreviation: WBC = white blood cell.  
† Data were available for 33 patients.  
‡ Data were available for eight patients.  
§ Data were available for 25 patients.
culture (obtained after 3 days of treatment) was negative. The *Haemophilus influenzae* infection was initially treated with intravenously administered cefotaxime, and the shunt system was left in place. After 6 days and persistent growth, the intraventricular catheter was externalized and intraventricular gentamicin treatment was added to the regimen. The CSF culture was positive after one instillation but became negative after the second. The β-hemolytic streptococcal infection was treated with intraventricularly administered vancomycin and intravenous cloxacillin. The culture was negative after two instillations.

**Duration of Treatment**

The duration of treatment in relation to causative bacteria is shown in Table 4. Overall, intraventricular treatment was administered for a median of 8 days (range 3–17 days). The median duration of intravenous treatment, including that shown in Table 3, was 10 days (range 4–45 days). The median duration of intravenous treatment after the start of intraventricular instillation, when cultures were all positive, was 7.5 days (range 4–16 days). Although intraventricular treatment was continued, intravenous treatment was changed to orally administered antibiotic therapy before shunt replacement in four patients. In all but two cases, no further antibiotic treatment was given after the day of shunt replacement; in two cases oral antibiotic therapy was continued for 4 or 10 days.

**Relapse and Mortality Rates**

During the initial follow-up period of 6 months, there were no relapses and no deaths (95% CI for death: 0.00–10.1% [34 cases]; 95% CI for relapse: 0.00–10.9% [32 cases]). The CI for relapse was somewhat higher due to reinfection within 6 months in two children. In one child who had been treated for a coagulase-negative staphylococcal infection, sepsis due to *K. pneumoniae* resulted in a new shunt infection 1 week after the shunt replacement. In the other child a β-hemolytic streptococcal infection was followed by a new shunt infection caused by *S. aureus* after 1 month. The other two reinfections occurred 8 and 12 years after treatment. In the children without reinfection the inserted new shunts were still in place 6 months after treatment. With extended follow-up until April 2007 (range 3–15 years), there have been no other reinfections or relapses.

**Adverse Effects**

No adverse effects related to the intraventricular antibiotic treatment were reported.

### TABLE 3

Antibiotic concentrations and results of CSF cultures in four patients initially treated with intravenous antibiotic therapy alone with or without catheter externalization

<table>
<thead>
<tr>
<th>Bacterial Agent</th>
<th>Antibiotic</th>
<th>Dosage (mg/kg/day)</th>
<th>Duration of Treatment (days)</th>
<th>Catheter Externalization</th>
<th>Culture Result</th>
<th>Antibiotic Concentration (mg/L)</th>
<th>Albumin Concentration (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>K. pneumoniae</em></td>
<td>meropenem</td>
<td>120</td>
<td>14</td>
<td>at the thoracic level</td>
<td>+</td>
<td>0.7</td>
<td>657</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>cefotaxime</td>
<td>300</td>
<td>6</td>
<td>proximal to the valve</td>
<td>+</td>
<td>&lt;2</td>
<td>206</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>cloxacillin</td>
<td>100</td>
<td>14</td>
<td>proximal to the valve</td>
<td>+</td>
<td>&lt;10</td>
<td>638</td>
</tr>
<tr>
<td>coagulase-negative</td>
<td>vancomycin</td>
<td>60</td>
<td>37</td>
<td>at the thoracic level</td>
<td>+</td>
<td>1.2</td>
<td>33</td>
</tr>
<tr>
<td>staphylococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

In the present study the effect of an institutional management protocol was evaluated retrospectively. Different definitions of shunt infection have been used in the literature. In some studies the diagnosis has been based only on the CSF culture result, whereas in others the diagnosis has been based on the CSF inflammatory response without the requirement of a positive culture. In our study the diagnosis of a definite shunt infection required positive cultures as well as signs of an inflammatory CSF response. Thus the risk of our having included patients who did not actually have a shunt infection in our case series is very low. The four patients with incomplete records who were classified as having a suspected infection demonstrated systemic symptoms and findings that did not differ from those in patients with a definite diagnosis of shunt infection, so it is unlikely that their inclusion was erroneous. A special strength of this study is that only three surgeons have been responsible for the principal clinical management of all the cases, resulting in a high degree of adherence to the protocol. The only patients not treated according to the protocol were the 10 children in whom treatment was started with intravenous antibiotic therapy alone. Because growth was evident in the CSF cultures obtained in all these patients when treatment was initiated according to the protocol, their cases were all included in the analysis together with those in which patients received the standard treatment from the start.

A treatment regimen like ours, with the use of intraventricular antibiotics from the outset in combination with systemic treatment and shunt removal, was proposed several years ago, but data regarding the effect of intraventricular instillation are limited. In recent studies and reviews the option of administering antibiotic agents intraventricularly has often been left to the surgeon’s preference.

In a recent practice survey on the treatment of shunt infections caused by coagulase-negative staphylococci, *S. aureus*, or Gram-negative bacteria, 60, 64, and 68% of the answering pediatric neurosurgeons, respectively, recommended removal of the shunt and implantation of an EVD. The angled ventricular catheter was left in place in our patients until shunt replacement. This procedure was based on the belief that it might be hazardous to change the ventricular catheter if the ventricles were slit-like and the risk that the straight EVD catheter might press against the wall of the ventricle. Furthermore, it was considered plausible that a smaller operation would be advantageous unless outweighed by drawbacks, such as lower cure or higher infection relapse rates. Despite our leaving the ventricular catheters, cultures became negative after a median of 3 days (range 1–6 days).
TABLE 4
Duration of antibiotic treatment and interval between the first intraventricular dose and shunt replacement

<table>
<thead>
<tr>
<th>Causative Agent and Route of Treatment</th>
<th>Coagulase-Negative Staphylococci</th>
<th>S. aureus</th>
<th>P. acne w/o Bacteremia</th>
<th>Enterococci w/o Bacteremia</th>
<th>Gram-Negative Rods w/ Bacteremia</th>
<th>β-Hemolytic Streptococci w/ Bacteremia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>w/o Bacteremia</td>
<td>w/ Bacteremia</td>
<td>w/o Bacteremia</td>
<td>w/ Bacteremia</td>
<td>w/o Bacteremia</td>
<td>w/ Bacteremia</td>
</tr>
<tr>
<td>Variable</td>
<td>IV</td>
<td>IV/oral</td>
<td>IV</td>
<td>IV/oral</td>
<td>IV</td>
<td>IV/oral</td>
</tr>
<tr>
<td>no. of patients</td>
<td>14</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>median no. of days of intraventricular Tx (range)</td>
<td>8 (5–16)</td>
<td>7</td>
<td>8 (4–11)</td>
<td>11.5 (7–17)</td>
<td>8 (8)</td>
<td>10</td>
</tr>
<tr>
<td>no. of patients treated w/ IV ABx for ≥3 days before start of intraventricular Tx</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>median no. of days of IV Tx (range)</td>
<td>10</td>
<td>4</td>
<td>11</td>
<td>6 (45)</td>
<td>12</td>
<td>12 (12–17)</td>
</tr>
<tr>
<td>median no. of days of oral FU Tx before shunt replacement (range)</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>median no. of days between 1st intraventricular dose &amp; shunt replacement (range)</td>
<td>8</td>
<td>5 (16)</td>
<td>7</td>
<td>8 (4–11)</td>
<td>11.5</td>
<td>7 (12)</td>
</tr>
<tr>
<td>no. of patients w/ oral FU Tx after shunt replacement (duration in days)</td>
<td>0</td>
<td>1 (10)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

*ABx = antibiotic; FU = follow-up; IV = intravenous; Tx = treatment; — = not applicable.
† Two children were not shunt dependent. Time to withdrawal of the ventricular catheter has been included in the calculations.
It must be emphasized, however, that cultures were not obtained on a daily basis and therefore the true time to sterilization is probably shorter. Of the eight CSF samples obtained on Day 2, only one was positive. In the study by Kestle et al.,12 in which complete removal of shunt components was performed in more than 70% of the patients and CSF samples were obtained daily, time to sterilization can be calculated at a mean of 3.4 days. In another study by Pfaußler et al.,16 in five adult patients with intraventricular coagulase-negative staphylococcal external drain infections in whom the ventricular catheter was immediately replaced, intraventricular administration of vancomycin resulted in sterilization after 2 to 3 days. Thus, despite leaving the proximal ventricular catheter in place, our sterilization data compare well with, and may even be better than, those in the study by Kestle et al.,12 and are on the order of those reported by Pfaußler et al.16 In all of the cases in our study, the infections were eliminated during treatment. This result is on the order of, or even better than, the result from a recent study by Turgut et al.,21 which two of 31 children were not cured during treatment, which comprised removal of all shunt components in combination with intraventricular and systemic antibiotics.

Brown et al.7 have reported on the efficacy of the antibiotics administered systemically and intraventricularly with the shunt left in situ. Intraventricular antibiotics were instilled via a separate access device. In addition to the criteria used in our study, cure definition required absence of relapse within 6 months. Applying this definition, a cure rate of only 84% was found, which was less than the lower 95% CI limit of our results, even if our cure rate criteria were redefined to be similar to those Brown and colleagues used in their study. Because both the ventricular catheters were left in place in both regimens, adherence of the bacteria to the valve or distal catheter may offer one explanation of the difference. Another might be that CSF trough concentrations of vancomycin and gentamicin in the study by Brown et al. were maintained at less than 10 mg/L and less than 2 mg/L, respectively, whereas most of our patients demonstrated higher concentrations—that is, above 10 mg/L for both antibiotics. Unfortunately, Turgut et al.21 did not include any information about the doses of intraventricular antibiotics used in their study.

As in many other studies in which antibiotics were administered intraventricularly,7,4 no side effects of this treatment were observed in our study. Cases have been reported in which patients had CSF vancomycin levels greater than 100 mg/L without toxic symptoms.1,14,15 On the other hand, CSF eosinophilia and high CSF protein levels have also been reported in patients with high concentrations of vancomycin.7,8,17 According to our protocol, patients were not routinely evaluated for eosinophilia.

The 10 cases in which children were initially treated with intravenous antibiotics alone, with or without externalization of the system at the start of the treatment, demonstrate the limitations of this strategy: CSF cultures in these cases showed persistent growth although the infections involved susceptible bacteria and the duration of treatment ranged from 3 to 37 days (median 8 days). It must be emphasized, however, that to some extent our cases represent a negative selection because children who demonstrated improvement after being treated with this regimen would not have been referred to our hospital. Despite antibiotic therapy in the high doses recommended for treatment of bacterial meningitis,7,9,18 low CSF concentrations of antibiotics were found in these 10 patients (Table 3). Although the method for cloxacillin assay was not sensitive enough to test low CSF concentrations of relevance, the time point for analysis might not have been optimal, and the minimum concentration to kill causative bacteria in the presence of a foreign body was not known, these relatively low antibiotic concentrations may have been an important factor for the poor sterilization.

The low-grade inflammatory response, as demonstrated by the comparatively low CSF albumin concentration, may not allow antibiotics to pass into CSF to the same extent as in acute meningitis caused by more virulent bacteria.

Duration of intraventricular treatment was less than 10 days in most patients; the duration of systemic treatment was somewhat longer in some patients because it was begun before the initiation of intraventricular treatment. This treatment period is considerably lower than the durations of antibiotic therapy reported by Turgut et al.,21 and Kestle et al.,12 of 37 days and 17 days, respectively, and in the lower range of those reported in the studies of Whitehead and Kestle23 and Brown et al.14 Despite a relatively short duration of antibiotic therapy, no relapses occurred. In older studies relapse rates of 15% to as high as 52% have been reported.15 In the more recent studies by Kulkarni et al.16 and Kestle et al.,12 rates of relapse with the same organism of 12 and 17%, respectively, were observed. All these relapse rates are higher than the upper 95% confidence limit found in the present study.

The choice of intravenously administered cloxacillin and vancomycin as systemic treatment in our protocol was based on previous personal experience. Rifampicin has been proposed by others,24 and with its ability to penetrate in low-grade inflammation,10 it is theoretically a better choice. On the other hand, the poor penetration and low CSF concentrations of cloxacillin and vancomycin, and perhaps even more that of oral flucloxacillin, suggest that in some patients the need for systemic antibiotic therapy in the treatment of intraventricular infection may be low. Nevertheless, it must be emphasized that our data pertaining to nonstaphylococcal infections are limited, which suggests that if a prospective study were performed in which intraventricularly administered antibiotic medication was to be used as the sole antibiotic therapy in combination with shunt removal with or without the ventricular catheter being left in situ, enrollment should be restricted to patients with shunt infections that are caused by staphylococci without bacteremia, significant signs of systemic inflammatory response, computed tomography findings indicating ventriculitis, or local signs along the shunt system.

Conclusions

In summary, this treatment regimen involving the administration of intraventricular antibiotics in a relatively high dose in combination with systemic antibiotic therapy seems to be safe and effective, resulting in quick sterilization and low relapse and mortality rates despite the ventricular catheter being left in place and a short duration of therapy. The surgical procedure was simplified by the externalization proximal to the valve. Furthermore, because the duration of antibiotic treatment is the major factor determining the duration of hospital stay, this regimen may be associated with a significant reduction in the cost of treatment.
References