Risk Factors for Pediatric Ventriculoperitoneal Shunt Infection and Predictors of Infectious Pathogens

Matthew J. McGirt, Aimee Zaas, Herbert E. Fuchs, Timothy M. George, Keith Kaye, and Daniel J. Sexton

1Division of Infectious Disease, Department of Medicine, and 2Pediatric Neurosurgery Service, Division of Neurosurgery, Department of Surgery, Duke University Medical Center, Durham, North Carolina

Identification of risk factors for shunt infection and predictors of infectious pathogens may improve current methods to prevent and treat shunt infections. We reviewed data on 820 consecutive ventriculoperitoneal (VP) shunt placement procedures in 442 pediatric patients at our institution during 1992–1998. Ninety-two shunts (11%) developed infection a median of 19 days (interquartile range, 11–35 days) after insertion. Premature birth (relative risk [RR], 4.81; 95% confidence interval [CI], 2.19–10.87), previous shunt infection (RR, 3.83; 95% CI, 2.40–6.13), and intraoperative use of the neuroendoscope (RR, 1.58; 95% CI, 1.01–2.50) were independent risk factors for shunt infection. The bacterial organisms early after shunt surgery (<14 days) were the same as those late after shunt surgery (>14 days). As determined by an analysis of the 92 infected shunts, hospital stay of >3 days at the time of shunt insertion (odds ratio [OR], 5.27; 95% CI, 1.15–25.3) and prior Staphylococcus aureus shunt infection (OR, 5.91; 95% CI, 1.35–25.9) independently increased the odds that S. aureus was the causal pathogen.

In the United States, hydrocephalus accounts for 70,000 hospital admissions each year [1]. Approximately 18,000 CSF shunts are placed per year, costing $100 million annually [1]. Thirty percent to 40% of all CSF shunts placed in pediatric patients fail within 1 year [2–10]. The ratio of shunt revisions to primary shunt placements remains 3:1 at many health care centers [11–13]. Many patients will undergo up to 14 shunt revisions in their lifetime [8, 10, 14–16].

CSF shunt infection is a common cause of shunt failure, with a reported incidence of 5%–15% [8, 10, 17–22]. Shunt infection is associated with an increased risk of seizure disorder, decreased intellectual performance, and a 2-fold increase in the long-term mortality rate [23, 24]. Reported risk factors for CSF shunt infection include etiology of hydrocephalus [25, 26], patient age [18, 27–29], previous shunt failure [18], and duration of shunt surgery [19, 30]. However, it is difficult to apply such findings to widely differing pediatric populations, because most of the preceding studies did not examine the confounding effects of patient characteristics on the risk of infection. The authors of a recent study reported that premature birth, postoperative CSF shunt leak, and intraoperatively breached gloves were independent risk factors for CSF shunt infection [31].

Staphylococcus aureus and coagulase-negative Staphylococcus species, a variety of gram-negative rods, Propionibacterium species, and Enterococcus faecalis are important causes of shunt infection [18, 28, 32, 33]. However, prior studies have not sought to identify clinical characteristics that are independently associated with shunt infections due to specific pathogens; as a result, clinical suspicion of the identity of the bacterial pathogen remains largely dependent on the individual
experience of the physician. We conducted a retrospective study of 820 consecutive ventriculoperitoneal (VP) shunt placement procedures at our institution with the goals of (1) identifying independent risk factors for CSF shunt infection, and (2) identifying independent clinical predictors of the causal bacterial pathogen.

MATERIALS AND METHODS

Patient population and treatment. All shunts were placed by 1 of 2 pediatric neurosurgeons who preferentially placed ventricular catheters via an occipital approach. Standards of practice that did not change during the study period included the following: nafcillin (25 mg/kg) or vancomycin (10 mg/kg) was administered immediately before the skin incision and again 12 h and 24 h after surgery; a 5–10-min skin preparation was performed using povidone-iodine scrub solution, isopropyl alcohol, and povidone-iodine paint (Duraprep); and adherent povidone-iodine–impregnated plastic drapes were placed over the incisions and tunneling sites. Before August 1995, all ventricular shunt catheter placements were performed without the use of a neuroendoscope; thereafter, a neuroendoscope was used to aid the placement of ventricular catheters in >98% of cases.

Standard follow-up consisted of clinical examination at 1 week, 1 month, 3 months, and yearly thereafter following the procedure. Head CT was performed on a yearly basis after shunt placement for all patients. Patients who presented with signs and symptoms of ventriculitis or meningitis were analyzed collectively as patients with shunt infection. As described elsewhere, criteria for CSF shunt infection were as follows: CSF culture that yielded a pathogenic organism or indicated CSF pleocytosis (leukocyte count, >50 leukocytes/mm³) associated with fever (temperature, >38.5°C), shunt malfunction, or neurological symptoms [19, 34]. The presence of incisional surgical site infection (SSI) was determined using the definitions of the National Nosocomial Infection Surveillance System [35]; SSIs that occurred >30 days after surgery were included in the calculation of rates of SSI. If criteria for shunt infection were met, the infected shunt was removed, an external ventricular drain was placed, and empirical vancomycin treatment (10 mg/kg iv q6h) was initiated. CSF specimens were obtained for culture via the shunt on the day of presentation and at least every other day thereafter until response to therapy was documented. New VP shunts were inserted only after CSF pleocytosis had resolved.

Data collection and statistical analysis. We reviewed the records for all pediatric patients who had VP shunts inserted for treatment of hydrocephalus during the period of January 1992 through December 1998. The following data were retrospectively collected from patient records: patient age and sex, etiology of hydrocephalus, date of shunt placement, number of prior shunt revisions, intraoperative use of a neuroendoscope, duration of hospital stay at the time of shunt insertion, history of prior shunt infection, administration of chemotherapy or radiation therapy ≤2 months after shunt placement, date of shunt infection, results of cultures of CSF or wound samples, and date of the most recent follow-up. A gestational age of <36 weeks was considered premature. Only shunts placed within the first 3 months after a premature birth were classified as “shunt placement in a premature neonate.”

Univariate comparison of time to shunt infection was assessed using Kaplan-Meier plots and log-rank analysis, for stratified covariates, and Cox proportional hazards analysis, for continuous covariates. A multivariate proportional hazards regression model was then created to model shunt infection hazard; the model included factors that had P values of <.1 on univariate analysis. Variables that demonstrated a P value of >.1 on multivariate analysis were removed from the model. Because our unit of analysis was the surgical procedure (as opposed to the patient), it was necessary to extend the Cox model to account for the fact that individual patients may have undergone multiple surgical procedures if they had experienced multiple shunt failures [36]. Conditional risk set techniques described by Prentice et al. [37] and Cleves [38] and used by Tuli et al. [16] were used for proportional hazards modeling. The procedures “stset” and “stcox” on Stata software (Stata) were used for conditional regression modeling [39]. Shunts were assigned a level according to the order that they were placed relative to revision surgery. The influence of underlying diagnosis on shunt failure was assessed using indicator variables. Each resultant model was clustered on shunt order.

Independent associations between clinical variables and the infective pathogen were assessed using a multivariate logistic regression model (SAS Logistic procedure on SAS software, version 8.2; SAS Institute [40]) adjusting for shunt order for the 92 infected shunts observed during the observational period. Only variables that demonstrated a P value of <.1 on univariate analysis were included in the multivariate logistic regression model.

RESULTS

Patient population. A total of 820 VP shunts were inserted in 442 pediatric patients. Fifty-two percent of the shunts were placed in male patients. The mean age of the patients was 7.6 years (range, 1 day to 18 years). The etiology of hydrocephalus was as follows: congenital/idiopathic, for 286 shunt insertions (35%); myelodysplasia, for 243 (30%); intraventricular hemorrhage (IVH), for 186 (23%); and tumor, for 105 (13%). A total of 472 shunts (58%) were placed with endoscopic assistance. Patients had a mean of 1 (range, 0–12) previous shunt insertion before the most recent shunt placement; 93 shunts...
(11%) were inserted to replace previously infected shunts. Nineteen VP shunts (2.3%) were inserted in premature neonates. Seventeen shunts (2.1%) were inserted ≥8 weeks after completion of chemotherapy. The median duration of follow-up was 3 years (interquartile range [IQR], 2–4 years) for all patients.

Ninety-two shunts (11%) became infected a median of 19 days (IQR, 11–35 days) after insertion. Culture of CSF specimens yielded coagulase-negative Staphylococcus species in 49 (53%) of 92 cases of shunt infection; S. aureus, in 24 cases (26%); gram-negative rods, in 8 cases (9%); and Propionibacterium species or E. faecalis, in 4 cases (4%). Culture results were negative for 7 infected shunts (8%).

### Risk factors for shunt infection.

Patients with shunt infections were more likely to be premature (P = .0001) and younger (P = .0003), had a greater number of prior shunt revisions (P = .0001), and were more likely to have had previous shunt infection (P = .0001) and to have had a shunt inserted with use of a neuroendoscope (P = .01); they were also more likely to have had IVH (P < .01) and less likely to have had tumor (P = .02) as the etiology of hydrocephalus (table 1). There were 4 independent risk factors for shunt infection. Insertion of a VP shunt in a premature neonate was associated with a nearly 5-fold increase in the risk of shunt infection (P<.01). Each decreasing year of patient age was associated with a 4% increase in the risk of shunt infection (P = .02). Intraoperative use of a neuroendoscope for shunt insertion increased the risk of shunt infection 1.6-fold (P = .05). Insertion of a shunt after a previous shunt infection was associated with a nearly 4-fold increase in the risk of shunt infection (P<.01), but it was not associated with an increased risk of overall shunt failure (relative risk, 1.23; 95% CI, 0.91–1.66; P = .17). Although significant on univariate analysis, IVH (P = .29) and tumor (P = .14) as etiologies of hydrocephalus were not significantly associated with shunt infection on multivariate analysis (table 2).

### Predictors of infection due to Staphylococcus species.

A previous shunt infection was documented in 31 patients who had shunt infections, and a pathogen was isolated from 27 of these 31 patients. Seventeen (63%) of these 27 patients were infected with an identical pathogen. A prior shunt infection caused by S. aureus increased the likelihood that S. aureus was the causal pathogen for the present infection (OR, 8.92; 95% CI, 2.08–38.2) and predicted that S. aureus would be the subsequent pathogen (positive predictive value, 70%; negative predictive value, 79%). A prior shunt infection caused by coagulase-negative Staphylococcus species did not increase the likelihood that the subsequent shunt infection was caused by coagulase-negative Staphylococcus species (OR, 1.95; 95% CI, 0.61–6.23). A hospital stay of ≥3 days before shunt insertion increased the likelihood that S. aureus was the causal pathogen (OR, 7.24; 95% CI, 1.57–33.4; positive predictive value, 35%; negative predictive value, 93%). A prior shunt infection caused by S. aureus (OR, 5.91; 95% CI, 1.35–25.9) and a hospital stay of ≥3 days before shunt insertion (OR, 5.27; 95% CI, 1.15–25.3) were independently associated with subsequent S. aureus shunt infection on multivariate analysis.
of surgery; increased complexity of the procedure, necessitating for the observed association between neuroendoscope use and ciation has not been previously demonstrated. Possible reasons creased risk of shunt infection. To our knowledge, this asso- pllication for the finding that the majority of shunt infections at the time of shunt insertion. This hypothesis is the best ex- mical opinion that, in most cases, the infecting agent is introduced after shunt insertion; this is consistent with the prevailing clin- In our patients, shunt infections occurred a median of 19 days at our health care center; this rate is consistent with accepted prior infection with a coagulase-negative species were the most commonly isolated pathogens, prior infection with a coagulase-negative Staphylococcus species was not predictive of subsequent shunt infection with a coagulase-negative Staphylococcus species.

Shunt infections occurred for 92 (11%) of 820 shunts placed at our health care center; this rate is consistent with accepted rates of pediatric VP shunt infection at other institutions [41]. In our patients, shunt infections occurred a median of 19 days after shunt insertion; this is consistent with the prevailing clinical opinion that, in most cases, the infecting agent is introduced at the time of shunt insertion. This hypothesis is the best explanation for the finding that the majority of shunt infections were due to skin flora. Methicillin-resistant Staphylococcus aureus caused only 5 shunt infections at our hospital, despite a high rate of previous hospitalization among patients in our cohort (data not shown). Premature birth was independently associated with VP shunt infection in our case series—a finding consistent with reports by previous investigators [18, 27–29, 31]. This association may be explained by the poorly developed immune system, immaturity of the skin, and the high density of bacteria on the skin characteristic of premature infants [42].

Use of a neuroendoscope was also associated with an increased risk of shunt infection. To our knowledge, this association has not been previously demonstrated. Possible reasons for the observed association between neuroendoscope use and increased risk of VP shunt infection include increased duration of surgery; increased complexity of the procedure, necessitating endoscopic guidance; and contaminated endoscopic equipment. The latter 2 explanations are unlikely in our case series, because, for almost all patients who had shunts placed after August 1995, a neuroendoscope was used for the procedure, regardless of the complexity of the surgery, and there was no evidence of an outbreak of infection around the time of ini- tiation of neuroendoscope use. In complex cases of hydro- cephalus involving neuroendoscope-assisted shunt insertion, however, the neuroendoscope was often used to break up adhesions or to fenestrate septum pellucidum. This may have contributed to the increased duration of the operation and subsequent infection. We were not surprised to find that pre- vious shunt infection increased the risk of subsequent shunt infection. Investigators have previously reported that the rate of shunt infection in patients undergoing reinsertions after re- moval of infected shunts (17.5%) was approximately twice as high as the overall rate of shunt infection (7.9%) [18].

We were also not surprised to find that prior shunt Staphylococcus infection or prolonged hospitalization before shunt insertion were predictive of subsequent shunt infection with Staphylococcus aureus. However, we were surprised to find that prior infection with coagulase-negative Staphylococcus species did not predict subsequent infection with coagulase-negative Staphylococcus species. These data suggest that closer follow-up and/or longer courses of treatment may be necessary for patients with Staphylococcus aureus shunt infection before shunt reinsertion is attempted.

VP shunt infection in the pediatric patient population re- mains a vexing problem. The types of pathogens encountered in patients in our case series justify the continued empirical use of vancomycin for treatment of suspected shunt infection. Additional prospective studies should examine whether operative use of a neuroendoscope is safe and appropriate for pre- mature patients or patients with a prior history of infection, or whether neuroendoscopes should be used only for technically difficult cases. In addition, further studies are necessary to determine whether longer courses of antimicrobial therapy can reduce the risk of relapse of Staphylococcus aureus infection or re- infestation in patients who undergo shunt revisions after treatment of Staphylococcus aureus shunt infections.

References

Table 2. Independent risk factors for CSF shunt infection in pediatric patients, as determined with a multivariate Cox model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative risk (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.04 (1.01–1.08)</td>
<td>.0168</td>
</tr>
<tr>
<td>Premature birth</td>
<td>4.81 (2.19–10.87)</td>
<td>.0002</td>
</tr>
<tr>
<td>Intraoperative use of neuroendoscope</td>
<td>1.58 (1.01–2.50)</td>
<td>.0508</td>
</tr>
<tr>
<td>Prior shunt infection</td>
<td>3.83 (2.40–6.13)</td>
<td>.0001</td>
</tr>
</tbody>
</table>

NOTE. We adjusted for shunt number in the multivariate logistic regression model.

<sup>a</sup> Decreasing age in years.