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Duration of Antibiotic Therapy and Timing of Shunt Reimplantation in Pediatric CSF Shunt Infections: A Retrospective Multicenter Case Series

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ORIGINAL ARTICLE

Duration of Antibiotic Therapy and Timing of Shunt Reimplantation in Pediatric CSF Shunt Infections: A Retrospective Multicenter Case Series

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In this retrospective multicenter series of 154 children with cerebrospinal fluid shunt infections, the median (interquartile range) duration of antibiotic therapy was 18 (14-26) days. The time to shunt replacement was 14 (10-19) days. Management appeared to potentially differ according to the targeted pathogen and site.

Key words: antibiotic duration; CSF shunt infection; shunt reimplantation.

Infection occurs as a complication of cerebrospinal fluid (CSF) shunt implantation in 7%-15% of patients [1, 2]. Infectious Diseases Society of America (IDSA) clinical practice guidelines for the management of shunt infections [3] propose that the duration of antimicrobial therapy be based on the pathogen, evidence of inflammation based on CSF findings, and extent of infection as defined by persistently positive cultures after removal of infected hardware [3]. Removal of infected shunt hardware is recommended, with temporary insertion of an external ventricular drain (EVD) until a new shunt can be placed [3]. The suggested timing of shunt reimplantation depends on the isolated organism, the CSF inflammatory parameters, and the rapidity of CSF sterilization [3]. To the best of our knowledge, there are no controlled trials or studies comparing different durations of antimicrobial therapy or time to shunt reimplantation.

The objective of this study was to describe current practices and outcomes in the management of CSF shunt infections in Canada and the United States, with a focus on the duration of antibiotic therapy and timing of CSF shunt reimplantation. Secondary objectives were to compare the observed duration of antibiotics and timing of shunt reimplantation with IDSA guidelines (published part-way through the study period) [3] and to investigate variability in clinical practice and outcomes between centers.

METHODS

Study Design

This retrospective multicenter case series was assembled by the Paediatric Investigators Collaborative Network on Infections in Canada (PICNIC) from pediatric tertiary care hospitals in Canada (n = 8) and the United States (n = 3). Ethics approval was obtained at each site.

Study Population

Inclusion criteria were: <18 years of age; CSF shunt in situ; infection, defined as growth of bacteria or fungi from CSF (sampled from shunt or lumbar puncture) or from the explanted CSF shunt tip from July 1, 2013 through June 30, 2019. Among patients with multiple shunt infections, only the first episode was included in the current study but all episodes up to June 30, 2019 were recorded to track reinfections. Exclusion criteria were microorganisms seen on Gram stain failed to grow in culture or the cultured organism was treated with antibiotics for 3 days or less, suggesting it was a contaminant.

Eligible patients were identified through the International Classification of Diseases (ICD) 10 codes

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(Supplementary Appendix) or microbiology laboratory databases. Study data were abstracted from the medical record using a standardized case report form by co-investigator physicians (9 sites) or by research assistants whom they supervised (2 sites) using REDCap electronic data capture tools hosted at the University of Alberta [4].

Definitions

Reinfection was defined as any other shunt infection during the study period. Relapse was defined as reinfection with the same pathogen within 60 days after stopping antibiotic therapy for the prior infection. Complications included contiguous soft tissue infection, worsening hydrocephalus, CSF leak, intracranial bleed, brain abscess, venous thrombosis, EVD infection, reinfection of new CSF shunt, relapse, and death. If the patient died, the physician completing the case report form was asked to judge whether the death was definitely attributable, possibly attributable, or unrelated to the shunt infection.

Data Analysis

Descriptive statistics included the number and percentage of cases (binary and categorical variables) and median and interquartile range (IQR, continuous variables). To examine variability between pathogens and between sites, the Kruskal-Wallis test and the chi-square test were used for continuous and categorical variables, respectively.

RESULTS

There were 154 patients who fulfilled the study criteria (Supplementary Table 1).

Antibiotic Treatment

Antibiotics were administered prior to CSF culture results in 137/154 patients (89%); vancomycin was used in 110 (80%) and an anti-pseudomonal agent in 51 (37%). Antibiotics were then tailored to the cultured pathogen. The median duration of antibiotic therapy was 18 days (IQR 14-26). With respect to gram-negative bacilli, the median treatment duration was 26 days (IQR 22-55) and 18/22 (82%) were treated for 21 days or more. Most received a longer course than outlined in IDSA guidelines [3] (Table 1). Treatment duration appeared to potentially vary according to the targeted pathogen and between participating centers (Supplementary Figure 1).

Among patients who had an EVD placed and reimplantation of a CSF shunt, antimicrobial therapy continued beyond shunt reinsertion in 75/112 (67%). This included 38/75 patients (51%) for whom the antibiotic duration was already extended beyond the recommended duration when the new shunt was placed.

Table 1. Recommendations [3] for Antibiotic Treatment Duration and Comparison to Observed Duration (N = 146[a])

No.[b]	Pathogen and Scenario	Recommended Duration of Therapy	Observed Duration of Therapy, Median (IQR)	Number of Cases
58	Coagulase-negative staphylococci or *C. acnes* without CSF abnormalities, few clinical symptoms	10 days	16 (12-24) days	7
59	Coagulase-negative staphylococci or *C. acnes* with CSF abnormalities or significant clinical symptoms	10-14 days	15 (13-18) days	32
60	*S. aureus* or gram-negative bacilli	10-14 days[f]	19 (16-32) days	32
61	Repeatedly positive cultures on appropriate antibiotics[c]	10-14 days after sterilization of CSF	18 (14-26) days after sterilization of CSF[d]	45
	Other[e]	No recommendation	15 (12-22) days	30

Abbreviations: CSF, cerebrospinal fluid; IDSA, Infectious Diseases Society of America; IQR, interquartile range.

[a]Data on duration of antibiotics were missing in 8 cases.

[b]Recommendation number (from 2017 IDSA guidelines [3]).

[c]Includes cases of coagulase-negative staphylococci or *C. acnes* (n = 12), *S. aureus* or gram-negative bacilli (n = 23), and other organisms (n = 14) with positive cultures after shunt removal.

[d]Median time to sterilization of CSF after shunt removal: 3 days (IQR 2-6).

[e]Includes other gram-positive, fungal, and polymicrobial infections.

[f]Some experts suggest treatment of infection caused by gram-negative bacilli for 21 days (weak recommendation, low quality of evidence).

Table 2. Recommendations [3] for Timing of CSF Shunt Reimplantation and Comparison to Observed Practice (N = 112[a])

No.[b]	Pathogen and Scenario	Recommended Timing of Reimplantation	Observed Timing of Reimplantation, Median (IQR)	Number of Cases
70	Coagulase-negative staphylococci or *C. acnes* without CSF abnormalities, negative culture after shunt removal	3 days after shunt removal	11 (8-16) days after shunt removal	5
71	Coagulase-negative staphylococci or *C. acnes* with CSF abnormalities, negative culture after shunt removal	7 days after shunt removal	11 (10-15) days after shunt removal	23
71	Coagulase-negative staphylococci or *C. acnes*, positive culture after shunt removal	7-10 days after sterilization of CSF	12 (7.8-13) days after sterilization of CSF[c]	8
72	*S. aureus* or gram-negative bacilli	10 days after sterilization of CSF	14 (12-16) days after sterilization of CSF[d]	43
	Other[e]	No recommendation	15 (9-24) days	33

Abbreviations: CSF, cerebrospinal fluid; EVD, external ventricular drain; IDSA, Infectious Diseases Society of America; IQR, interquartile range.

[a]Only patients with shunt removal, EVD placement, and shunt later replaced (n = 112) were included in the analysis of shunt reimplantation.

[b]Recommendation number (from 2017 IDSA guidelines [3]).

[c]Median time to sterilization of CSF after shunt removal of 1.5 days (IQR 1.0-3.8).

[d]Includes 23 patients who did not have any positive culture documented after shunt removal in whom sterilization of the CSF was considered the date of shunt removal and 20 patients with positive cultures after shunt removal and median time to sterilization of CSF after shunt removal of 3.5 days (IQR 2-5).

[e]Includes other gram-positive, fungal, and polymicrobial infections.

Surgical Management

The shunt was completely removed in 145/154 (94%) patients. In the remaining cases, a portion of the shunt was externalized (n = 6, 3.9%), or retained (n = 3, 1.9%). Among patients with complete shunt removal, a temporary EVD was placed and a new, permanent shunt was eventually inserted in 112/145 (77%) patients. The median time between removal of the shunt and reimplantation was 14 days (IQR 10-19) and was usually longer than proposed in IDSA guidelines [3] (Table 2). Variability in time to shunt reimplantation based on the isolated microorganism and center are shown in Supplementary Figure 1.

Outcomes

Sixty-two of 154 patients (40%) had one or more complications (Supplementary Table 1). There were three EVD infections (with methicillin-susceptible *Staphylococcus aureus* [MSSA], 10 days after insertion; *Enterococcus faecalis* after 35 days; and *Candida parapsilosis* after 16 days). There was one relapse (with methicillin-resistant *Staphylococcus aureus*). Seventeen other patients (11%) had one or more reinfections during the study period. Nine (5.8%) children died, with four of the deaths definitely attributed to the shunt infection.

DISCUSSION

Our findings underscore significant practice variability in duration of antibiotic therapy and timing of shunt reimplantation with most patients receiving longer treatment courses and delayed shunt reimplantation when compared to IDSA recommendations [3].

Almost all patients (94%) had complete removal of the infected shunt, as compared to 81% in a 2008-2012 study at primarily US sites [5]. The median antibiotic duration in the current study (18 days; IQR 14-26) is similar to culture-positive patients in the previous study (19 days, IQR 12-28 days) [5].

In the current study, practitioners tended to treat infections with *Pseudomonas aeruginosa*, other gram-negative bacilli, and yeast for longer durations than other pathogens (Supplementary Figure 1A). IDSA guidelines suggest treatment of infection caused by gram-negative bacilli for 21 days (weak recommendation, low-quality evidence) [3]. Continuation of antibiotics beyond shunt reimplantation is recommended only if the patient has not yet completed the suggested duration of antibiotics [3]. In our study, 67% of antibiotic courses continued after shunt reimplantation (vs only 23% in a previous study [5]), half of which exceeded the suggested total duration of antibiotics. Previous studies have shown no evidence for increased reinfection with shorter total durations of antibiotics but did not distinguish between relapse and other reinfections [6–8].

With respect to the timing of insertion of a new CSF shunt, practice variability between hospitals was apparent (Supplementary Figure 1D). Comparison to IDSA guidelines showed that, in most cases, the shunt was reimplanted later than recommended (Table 2) [3]. Timing of the surgical procedure may depend on factors external to the patient such as operating room availability. Differences in pediatric vs adult practice may also explain some of the discordance with IDSA guidelines. Similar to previous studies [7, 8], our series does not provide evidence of a causal association between timing of reinsertion and clinical outcomes.

One limitation is that cases could have been missed, particularly in sites that used only ICD 10 codes and not microbiology databases. Culture negative cases were not included while some included cases might have represented contaminated cultures. Inter-rater reliability for data collection was

not assessed. The observational, retrospective design limited our ability to draw causal inferences. An informative study would include enough cases of sub-optimal therapy to measure a difference in outcomes whereas our ability to do so is hindered by having only four deaths and one relapse. This suggests that clinicians are cautious in the management of shunt infections in children. Although outcomes were generally good, shorter treatment duration would have benefits if good outcomes can be maintained. Our series was heterogeneous with respect to the type of shunt, surgical management, isolated organism, patient co-morbidities, and other factors. Subgroup analyses would be of interest but were limited by the sample size. With a larger sample size, we could have compared management before and after the publication of IDSA guidelines.

In summary, our case series provides a representative picture of the population of complex pediatric patients with CSF shunt infections managed by pediatric infectious diseases clinicians at North American hospitals. The antibiotic treatment duration and the interval from explantation of an infected shunt to reinsertion of a new shunt often exceeded the recommended duration in practice guidelines [3]. Although these data neither support nor challenge current management guidelines, they highlight significant uncertainties in key management issues, which can only be answered by future well-powered controlled trials.

Supplementary Data

Supplementary materials are available at the *Journal of the Pediatric Infectious Diseases Society* online.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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