Variation in Duration of Antibiotic Therapy for Central-line Associated Blood Stream Infections Caused by Gram Negative Bacilli in Hospitalized Children

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Introduction

- Central-line associated bloodstream infections (CLASBIs) are associated with significant morbidity, mortality, and cost.[1,2]
- Current treatment guidelines recommend treatment duration of 7-14 days for CLABSIs caused by Gram-negative bacilli (GNB),[3] with significant practice variation seen.
- The optimal length of therapy for children with CLASBIs caused by GNB is unknown.
- The purpose of this study was to examine the variation in length of therapy in children with Gram-negative CLABSIs and its association with treatment failure.
- We hypothesized that duration of effective antibiotic therapy would not be associated with higher rates of microbiological recurrence within 365 days.

Methods

- A retrospective cohort study was performed on all patients diagnosed with CLABSIs at Ann & Robert H. Lurie Children's Hospital of Chicago, a 288-bed tertiary care academic children's hospital, from June 2008 through September 2019.
- Patients with polymicrobial BSIs, osteomyelitis, endocarditis, and death before completion of treatment of BSI were excluded.
- CLABSIs were defined as per the NHSN criteria. [4]
- The primary exposure variable was duration of effective therapy, defined as continuous calendar days of an antibiotic(s) to which the GNB was susceptible, from date of microbiological clearance.
- The primary outcome was microbiological recurrence defined as recurrent BSI with the same organism after the end of the treatment period, but within 365 days of the index BSI.
- Resistant organisms were defined by resistance to any 3rd or 4th generation cephalosporin or piperacillin/tazobactam, or any extended-spectrum beta-lactamase production.
- Additional covariates included presence of severe neutropenia, short bowel syndrome, immunocompromised status (hematopoietic stem cell/solid organ transplant, primary immunodeficiency), severe infection (new pressor requirement, transfer to ICU) and exit site infection; organism and antibiotic susceptibilities; and removal of catheter and use of antibiotic locks.
- Interquartile ratios were calculated for the lengths of therapy in those with and without line removal prior to the end of antibiotic therapy. Two-tailed Mann-Whitney tests were used to calculate the significance of differences in length of therapy between groups.

Results

Table 1. Characteristics of patients with CLABSIs caused by GNB.

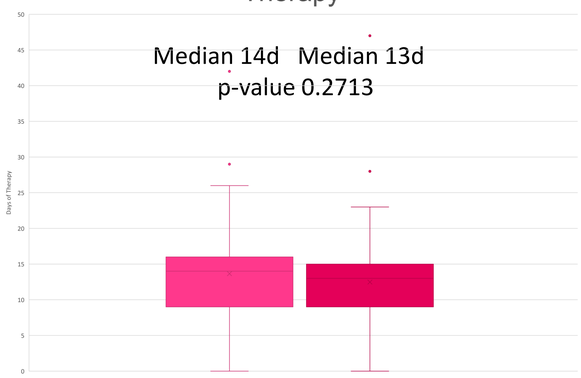
Patient Variable	N=94	% or IQR
Male	60	63.8%
Median Age (y)	2.95	0.74-11.14
Immunocompromised	61	64.9%
Stem Cell Transplant	29	30.9%
Solid Organ Transplant	4	4.2%
Other	28	29.8%
Short Gut	10	10.6%

Table 2. Description of CLABSI cases.

Variable	N=97	%
Severe Neutropenia	45	46.4%
Severe Infection	36	37.1%
Resistant Organism	37	38.1%
Catheter Removal	49	50.5%

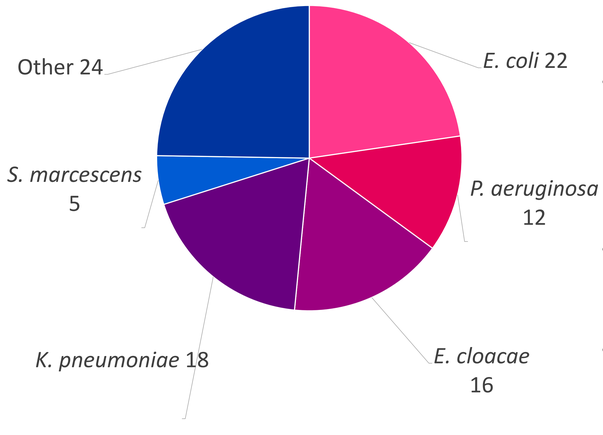
- 94 patients experienced 97 CLABSIs. In 49 (50.5%) infections, the central line was removed prior to the end of antibiotic therapy.
- Of the 97 cases, 6 had microbiological recurrence within 365 days of the end of therapy.
- Recurrence in one case was unknown.
- The median length of effective therapy in infections with recurrence was 11.17 days, compared to 13.29 days for those with no recurrence (p=0.2627).
- Of the six cases with microbiological recurrence, 3 retained their central lines throughout the course of therapy.
- The difference in length of therapy between the retained line and removed line groups in this cohort was not significant (p=.9647).

Figure 1. Length of Effective Antibiotic Therapy



Catheter removed prior to end of treatment (pink), or retained (red).

Figure 2. Pathogens Isolated from CLABSIs



Number of isolates indicated.

- *Enterobacteriaceae* were the majority of causative pathogens (n=63, 64.9%).
- Notable, less common pathogens isolated from the cohort included *Achromobacter xylosoxidans (n=2)*, *Prevotella melaninogenica (n=2), Leptotrichia trevisanii (n=1)*, and *Acinetobacter lwoffi (n=1)*.

Conclusions

- The relationship between catheter removal and microbiological recurrence was not clear, as recurrence occurred in only 6.2% of CLABSIs.
- Our observed catheter removal rate of 50.5% was higher than a recently reported study of pediatric CLABSIs (33%), which also reported a higher recurrence rate (13.9% vs 6.2%), although Gram-positive and yeast were also included.[5]
- Whether catheters were removed or retained, there was wide variation in the duration of antimicrobial duration for treatment of CLABSIs due to GNB.
- Differences in duration of therapy between patients with and with recurrence was not observed, however the limited number of recurrences prevented full conclusions from being drawn.
- Our results suggest potential stewardship interventions such as reducing length of therapy from 14 to 10 days.
- Very prolonged duration of therapy (>21 days) may have been for complications such as infected thrombi. Standardization of duration in these instances may be an additional stewardship target.
- The primary study limitation was the relatively few number of study outcomes observed.
- Future avenues of direction include the addition of other centers and multivariable analyses to account for patient comorbidities.

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