Poster #: 279

A Decision Tree Using Clinical Characteristics to Predict a Hospitalized Child's Risk of a Multidrug-Resistant Gram-Negative Bloodstream Infection

Anna C. Sick-Samuels, Katherine E. Goodman, Glenn Rapsinski, Elizabeth Colantouni, Aaron M. Milstone, Andrew J. Nowalk, and Pranita D. Tamma

Johns Hopkins University School of Medicine, Baltimore, MD, USA

Anna Sick-Samuels, MD, MPH
Department of Pediatrics
Division of Infectious Diseases
200 N. Wolfe Street, Office 3093
Baltimore, MD 21287
asick1@jhmi.edu

Introduction

Children with concern for bloodstream infections are often empirically started on broad-spectrum antibiotic agents such as cefepime or piperacillin.

Multidrug resistant Gram-negative (MDRGN) infections are a growing threat[1,2], and infections with MDRGN organisms are associated with a delay to appropriate antibiotics with poorer clinical outcomes[3-7].

Therefore, it is important to identify children who are at high-risk of a resistant infection and may benefit from broader empiric therapy from children who are at low risk of resistance and for whom standard empiric therapy is appropriate.

Clinical prediction tools have not previously been developed to predict the risk of increased Gram-negative organism resistance for pediatric patients.

Objective

To develop a user-friendly clinical decision aid for children identified to have a Gram-negative bloodstream infection to predict risk of resistance to common first-line empiric antibiotics of cefepime or piperacillin-tazobactam (pip-tazo).

Methods

Study design, population and definitions:

- A longitudinal retrospective cohort study
- All patients admitted to the Pittsburgh Children's Hospital from June 2009-June 2015 with Gram-negative bloodstream infection. Infection episodes considered unique if at least 30 days elapsed since a prior bloodstream infection.
- Primary outcome was a Gram-negative bloodstream infection with resistance to cefepime or pip-tazo.

Analysis:

- Risk factors explored with logistic regression accounting for longitudinal data.
- Pattern of resistance outcome explored over time for patients with multiple infections.
- A decision tree describing risk of an infection resistant to cefepime or pip-tazo developed using recursive partitioning.
- Validated using leave-one-out cross validation.

References

1. Logan LK, Braykov NP, Weinstein RA, et al. . J Pediatric Infect Dis Soc. 2014;3(4):320-328.
2. Logan LK, Gandra S, Mandal S, et al. JPIDS. J Pediatric Infect Dis Soc. 2017 Nov 24;6(4):352-35
3. Sick AC, Tschudin-Sutter S, Turnbull AE, et al. Pediatrics. 2014;133:e1148-1155.
4. Folgori L, Livadiotti S, Carletti M, et al. Pediatr Infect Dis J. 2014;33(9):929-932.
5. Kim YK, Pai H, Lee HJ, et al. Antimicrob Agents Chemother.. 2002;46(5):1481-1491.
6. Tumbarello M, Sanguinetti M, Montuori E, et al. Antimicrob Agents Chemother. 2007;51:1987-94.
7. Tamma PD, Han JH, Rock C, et al. Clin Infect Dis. 2015;60:1319-1325.

Results

- 689 episodes of Gram-negative bloodstream infections among 387 patients
- Overall 32% of bloodstream infections were cefepime or pip-tazo resistant
- Among patients with multiple infections, it was more likely that subsequent infection was cefepime or pip-tazo resistant if prior episode was also resistant (n=106) than if it was susceptible (n=196) (59% vs. 30%, p<0.001)

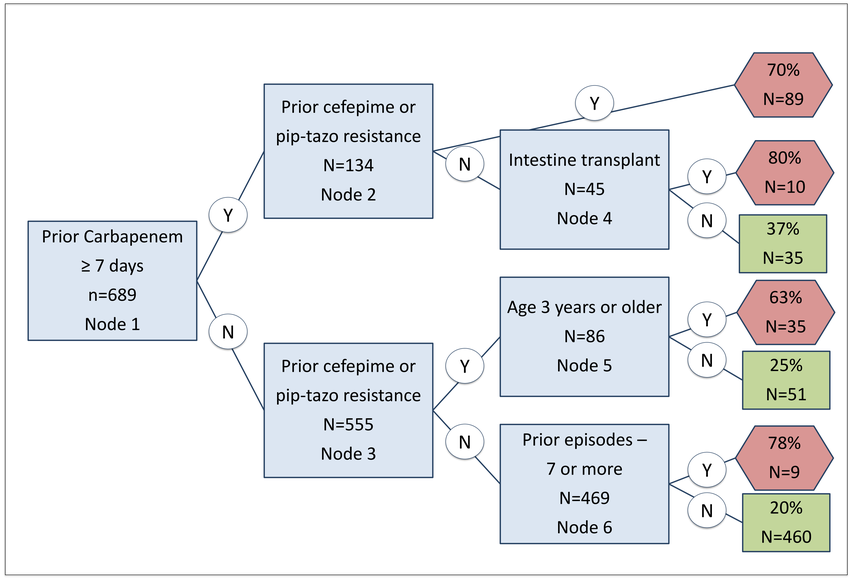

Figure 1. A decision tree illustrating the risk of having cefepime or piperacillin-tazobactam resistance among children with Gram-negative bloodstream infections based on individual patient risk factors. Risk of cefepime or piperacillin-tazobactam resistance presented as a percentage and stratified into high-risk (red) and low-risk groups (green). Y- yes; N- no.

Table 2. Tree Performance after Validation

Sensitivity	46%
Specificity	92%
Area under the curve	0.70
Positive predictive value	69%
Negative predictive value	78%

Table 1. Clinical Characteristics of children with Gram-negative bloodstream infections, by cefepime or piperacillin-tazobactam (CPT) resistance status.

Clinical Characteristics	Non-resistant N=472 (68.5%)	CPT- Resistant N=217 (31.5%)	Odds Ratio	95% Confidence Interval	
Female (%)	200 (42.4)	107 (49.3)	1.25	0.85	1.85
Age in years, median (IQR)	2.1 (0.7, 6.7)	3.7 (1.5, 9.8)	1.03	1.00	1.06
Born outside USA (%)	26 (5.5)	26 (12.0)	1.96	0.97	3.93
Pre-existing conditions (%)					
Malignancy	53 (11.2)	12 (5.5)	0.62	0.29	1.29
Bone marrow transplant	37 (7.8)	13 (6.0)	0.96	0.45	2.07
Congenital cardiac disease	24 (5.1)	7 (3.2)	1.03	0.41	2.60
Intestinal insufficiency	146 (30.9)	66 (30.4)	1.36	0.81	2.28
Intestinal transplant	38 (8.1)	55 (25.3)	3.55	2.04	6.16
Solid organ transplant	22 (4.7)	10 (4.6)	1.51	0.69	3.29
Other diagnosis	152 (32.3)	54 (24.9)	reference	reference	reference
Central line (%)	368 (78.0)	189 (87.1)	1.57	0.98	2.54
Vasopressors (%)	60 (12.7)	39 (18.0)	1.44	0.92	2.26
Admitted to ICU (%)	215 (45.6)	125 (57.6)	1.47	1.07	2.01
Culture with CPT-resistance within 6 months (%)	78 (16.5)	97 (44.7)	2.78	1.92	4.01
Months since a prior discharge, median (IQR)	0.0 (0.0, 2.0)	0.0 (0.0, 1.0)	1.00	0.96	1.04
Number of prior bloodstream infection episodes, median (IQR)	0.0 (0.0, 1.0)	1.0 (0.0, 3.0)	1.13	1.03	1.24
Days admitted prior to blood culture, median (IQR)	0 (0, 11.5)	1 (0, 20)	1.01	1.00	1.01
Antibiotic therapy ≥7 days within 6 months (%)					
3rd generation cephalosporin	63 (13.3)	24 (11.1)	1.01	0.62	1.65
Cefepime	105 (22.2)	53 (24.4)	1.21	0.80	1.83
Piperacillin-tazobactam	216 (45.8)	128 (59.0)	1.46	1.02	2.06
Carbapenem	51 (10.8)	83 (38.2)	4.20	2.78	6.33
Fluoroquinolone	45 (9.5)	37 (17.1)	1.41	0.88	2.26

Note: Additional variables included in decision tree input that are not shown above include race (White, Black, Asian and Other), Number of Prior admissions in categories (0, 1-4, 5-9, 10-14, 15 or more).

Conclusion

We developed a decision tree to provide individualized risk assessment of resistance to cefepime or pip-tazo when children are identified to have a Gram-negative bloodstream infection that may assist in empiric antibiotic selection.

Acknowledgements

We would like to thank John Gilmore, Ximin Li, the Pediatric Infectious Diseases faculty of the Children's Hospital of Pittsburgh, and the recognition of the Pediatric Infectious Diseases Society Antimicrobial Stewardship Fellowship Award. This work was supported in part by NIH grant T32 A1052071.