JOURNAL CLUB

Are You Going Overboard on Cephalosporins?

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The study

This prospective chart review study (2011–2013) from Texas included infants aged ≤60 days with a positive culture from the blood, urine, or cerebrospinal fluid. The researcher's objectives were to study the pathogens and the optimal choice of antibiotics in infants with serious bacterial infection (SBI).

The key findings

The study found 265 infants with SBI. Of those infants, 11% had meningitis, 25% had bacteremia or bacteremia with urinary tract infection, and 64% had urinary tract infection alone. *Escherichia coli* and group B *Streptococcus* were the predominate pathogens. There were no cases of methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, or penicillin-resistant *Streptococcus pneumonia*. For infants aged ≤28 days, the combination of ampicillin and gentamicin was used in 78% of cases, whereas a third-generation cephalosporin was used in 22% of cases. For infants aged ≥29 days, ampicillin and gentamicin were used in 13% of cases, and a third-generation cephalosporin was used in 87% of cases.

The authors noted that when meningitis was not suspected, regimens of either ampicillin/gentamicin or a third-generation cephalosporin were equally effective based on susceptibility data (96% and 97%). They also noted that 67% of cases in which a third-generation cephalosporin was used resulted in unnecessarily broad coverage compared with ampicillin/gentamicin. Also, 57% of third-generation courses were continued despite susceptibility results allowing deescalation of therapy.

Why do we care?

Hospitalized infants with fever and suspected SBI are our wheelhouse. We love third-generation cephalosporins, especially for infants aged 29 days and older. This study suggests that for infants in whom meningitis is not suspected, we should be using gentamicin instead of a cephalosporin to avoid antibiotic resistance. Our love for cephalosporins may also be preventing us from narrowing our coverage once susceptibilities are known.

STRAIGHT FROM THE AUTHOR …

We reached out to Dr J.B. Canty, the lead author of the study, and asked him these questions: What about gentamicin's side effects? and What about checking gentamicin levels? Here is his response:

"As user-friendly as third-generation cephalosporins can be, they come with a cost: exposure of the infant's normal gut flora to cephalosporins leads to both the development of drug resistance and the elimination of protective commensal organisms. In turn, this leads to increased infections with resistant organisms and yeast down the road. While these side effects are seen most easily in closed systems such as the neonatal intensive care unit, it is important to remember that the community is just a big closed system! The use of aminoglycosides has not been associated with these adverse outcomes. Admittedly aminoglycoside levels are an extra burden on the infant, but only those infants who have a culture-

www.hospitalpediatrics.org
DOI:10.1542/hpeds.2015-0234

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HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

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proven SBI that requires aminoglycoside therapy will require levels. For most infants, the empiric therapy will be discontinued or narrowed before levels are needed. Finally, third-generation cephalosporins are needed when meningitis is suspected, but it is critical to obtain cerebrospinal fluid before starting antibiotic therapy to prevent infants from being 'stuck' on unnecessarily broad cephalosporin therapy."

CITATION Cantey JB, Lopez-Medina E, Nguyen S, Doern C, Garcia C. Empiric antibiotics for serious bacterial infections in young infants: Opportunities for stewardship. *Pediatr Emerg Care*. 2015;31(8):568–571

VANCOMYCIN IN CONJUNCTION WITH OTHER NEPHROTOXIC AGENTS AND ACUTE KIDNEY INJURY

The study

This retrospective chart review looked to identify risk factors for acute kidney injury (AKI) in patients aged 3 months to 18 years treated with intravenous vancomycin while admitted to a tertiary care center between February 2009 and September 2010. AKI was defined as having a 50% decrease in estimated GFR during or up to 72 hours after vancomycin therapy. Patients were excluded if they received vancomycin for <48 hours, received vasopressors 48 hours before to 72 hours after vancomycin therapy, had a transplanted or solitary kidney, had tumor lysis syndrome, or lacked baseline laboratory data. Vancomycin dosing was studied rather than measured serum levels such that AKI independent of vancomycin causing an elevation in levels would not confound the results.

The key findings

Of the 175 patients included, 24 (13.7%) met AKI criteria. Odds of AKI markedly increased with coadministration of nephrotoxic medications (odds ratio [OR] = 5.02; 95% confidence interval [CI] = 1.09–23.19). Patients with AKI received a median of 1 (interquartile range = 0–2) nephrotoxic medication concurrently with vancomycin, whereas patients without AKI received a median of 0 concurrent nephrotoxic medications (interquartile range = 0–1; $P = .042$).

A multivariate regression showed that the likelihood of AKI increased with each 5-mg/kg increase in vancomycin dose (OR = 1.16; 95% CI = 1.01–1.33) and with each additional day of therapy (OR = 1.11; 95% CI = 1.01–1.22). In all models, concurrent use of nephrotoxic medications and longer durations of therapy were associated with increased odds of AKI.

Why do we care?

With higher vancomycin dosing for many infections after 2009 Infectious Diseases Society of America recommendations[1] and evidence mounting that even transient AKI in childhood is associated with deleterious effects later in life,[2] it is more important than ever to give forethought to prevention of AKI in children receiving vancomycin. As hospitalists, we should be at the center of quality improvement initiatives using systems of care to prevent harm. Potential avenues for improvement include prompts to discontinue antibiotics as soon as medically reasonable, changes to less toxic antibiotics, and avoidance of other nephrotoxic medications while prescribing vancomycin.

STRAIGHT FROM THE AUTHOR …

"Practices around vancomycin vary among institutions due to the lack of clinical outcomes data to guide dosing, trough targets, and monitoring. Until there are stronger clinical data it is difficult to define the optimal practice around vancomycin use. If we can use the shortest appropriate length of therapy and minimize concomitant use of other nephrotoxic medications as possible during vancomycin therapy, that may decrease the odds of AKI in those patients. Careful monitoring of kidney function, especially for patients on higher vancomycin doses or those receiving concurrent nephrotoxins, is important."

CITATION Sinclair EA, Yenokyan G, McMunn A, Fadrowski JJ, Milstone AM, Lee CK. Factors associated with acute kidney injury in children receiving vancomycin. *Ann Pharmacother*. 2014;48(12):1555–1562

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2. Greenberg JH, Coca S, Parikh CR. Long-term risk of chronic kidney disease and mortality in children after acute kidney injury: a systematic review. *BMC Nephrol*. 2014;15:184

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Hospital Pediatrics 2016;6;112
DOI: 10.1542/hpeds.2015-0234 originally published online January 1, 2016;

Hospital Pediatrics®
AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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DOI: 10.1542/hpeds.2015-0234 originally published online January 1, 2016;