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Editorial

Should we prescribe carbapenem for treating febrile urinary tract infection caused by extended-spectrum β-lactamase-producing *Enterobacteriaceae* in children with vesicoureteral reflux?

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Key message

Recent studies are focused on the noninferiority of noncarbapenem therapy for the treatment of extended-spectrum β-lactamases producing *Enterobacteriaceae* infections to reduce the utilization of carbapenem.

Urinary tract infections (UTIs) are the most common serious bacterial infections in children.[1] The most common pathogens causing UTIs are *Enterobacteriaceae*, such as *Escherichia coli* and *Klebsiella* species.[2] Antimicrobial drug resistance to fluoroquinolone, cephalosporin, and carbapenem among *Enterobacteriaceae* has spread globally over the past few decades and become a pressing problem.[3] The dissemination of drug-resistant organisms is troublesome for clinicians when selecting empirical antibiotics. Patients with UTIs were historically administered broad-spectrum cephalosporin as the empirical therapy. Carbapenem is the definitive therapy for infections caused by extended-spectrum β-lactamases (ESBL)–producing bacteria. However, carbapenem-sparing options are on the rise for mild infections with ESBL producers because its overuse is leading to the emergence of carbapenem-resistant organisms.

Recent studies have focused on the noninferiority of noncarbapenem therapy for the treatment of ESBL-producing *Enterobacteriaceae* infections to reduce carbapenem utilization.[4-7] A review article examined noncarbapenem β-lactam (cephamycin, cefepime, piperacillin/tazobactam, and newer β-lactam/β-lacta-

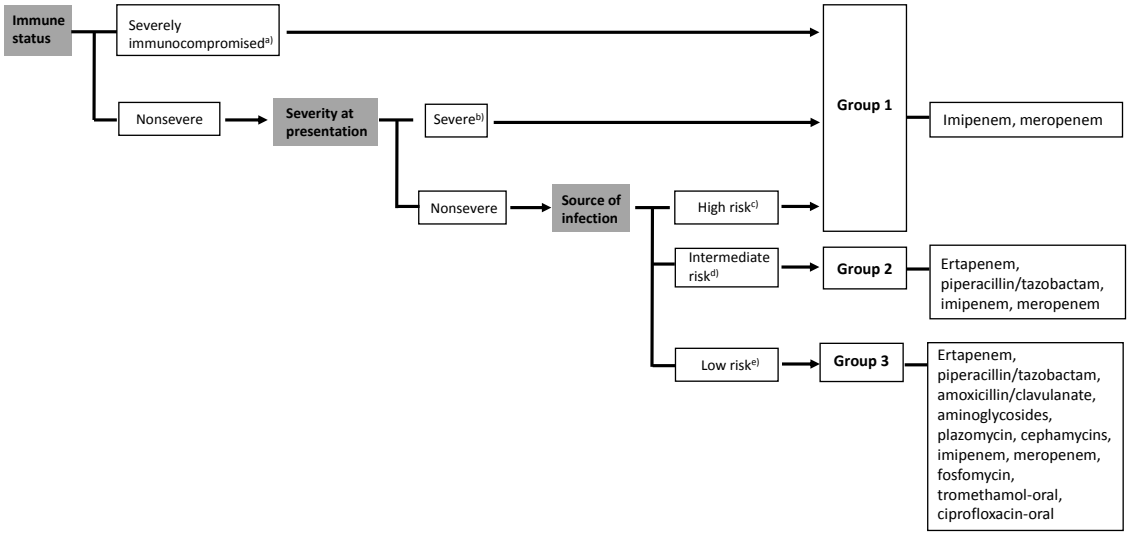

Fig. 1. Classification of patients according to immune status, severity at presentation, source of infection, and treatment options for infections caused by extended-spectrum β-lactamase-producing *Enterobacteriaceae* by group.[7] [a]Severely immunocompromised: neutropenia (<500/μL), leukemia, lymphoma, HIV infection with <200 CD4/μL, solid organ or hematopoietic stem cell transplantation, cytotoxic chemotherapy, steroids (15 mg of prednisone daily for >2 weeks); [b]Severe: Pitt score ≥4, Acute Physiology and Chronic Health Evaluation II score > 10, intensive care unit admission, and presentation with severe sepsis or septic shock; [c]High risk: high-inoculum infections, drainage impossible or inadequate (e.g., pneumonia, endocarditis, inadequately drained deep-seated infections); [d]Intermediate risk: not high or low risk; [e]Low risk: urinary tract infection with no or a released obstruction.

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mase inhibitors) therapy for ESBL-producing bacterial infections. The authors suggested that noncarbapenem could be considered in patients with mild to moderate low-inoculum infections.[6] A recent literature review summarized published articles regarding the treatment of ESBL-producing *Enterobacteriaceae* infections. Patients were divided into 3 groups: group 1, severe or nonsevere infections from high-risk sources and/or severely immunocompromised patients; group 2, nonsevere infections and intermediate-risk sources; and group 3, nonsevere infections and low-risk sources (Fig. 1). They concluded that carbapenem should be the choice of drug for the treatment of ESBL-producing *Enterobacteriaceae* in severe infections, whereas other antimicrobial agents could be considered for mild infections such as UTIs.[7] Thus, using noncarbapenem therapy for treating UTIs caused by ESBL-producing bacteria could be an effective way to prevent carbapenem overuse.

Furthermore, children with vesicoureteral reflux (VUR) are at high risk for acute and recurrent pyelonephritis.[8] In patients with VUR, it is unknown whether carbapenem therapy can reduce the short-term recurrence. Therefore, a prospective study is needed to compare the treatment outcomes of carbapenem-treated and non–carbapenem-treated patients diagnosed with UTIs due to ESBL producers underlying VUR. To enable a careful conclusion, large samples and multivariate analysis are required.

If UTIs caused by ESBL-producing bacteria are alleviated through empirical noncarbapenem therapy, switching to carbapenem therapy is a difficult decision for clinicians. To solve this challenge and develop management guidelines, additional large-scale randomized controlled trials are required.

Conflicts of Interest
No potential conflicts of interest for this article are reported.

See the article "Febrile urinary tract infection in children: changes in epidemiology, etiology, and antibiotic resistance patterns over a decade" via https://doi.org/10.3345/cep.2020.00773.

References

1. Lindsey K, Marianella H, John DS. The clinical diagnosis and management of urinary tract infections in children and adolescents. Paediatr Int Child Health 2017;37:273-9.
2. Zorc JJ, Kiddoo DA, Shaw KN. Diagnosis and management of pediatric urinary tract infections. Clin Microbiol Rev 2005;18:417-22.
3. Amy JM, Giswlw P, Johann DDP. The role of epidemic resistance plasmids and international high risk clones in the spread of multidrug-resistant Enterobacteriaceae. Clin Microbiol Rev 2015;28:565-91.
4. Lee B, Kang SY, Kang HM, Yang NR, Kang HG, Ha IS, et al. Outcome of antimicrobial therapy of pediatric urinary tract infections caused by extended-spectrum β-lactamase-producing Enterobacteriaceae. Infect Chemother 2013;45:415-21.
5. Yoshifusa A, Isil IE, Kunihiko F, Hitomi W, Yasuha O, Satoshi H, et al. Efficacy of non-carbapenem antibiotics for pediatric patients with first febrile urinary tract infection due to extended-spectrum beta-lactamase-producing Escherichia coli. J Infect Chemother 2017;23:517-22.
6. Pranita DT, Jesus RB. The use of noncarbapenem β-lactams for the treatment of extended-spectrum β-lactamase infections. Clin Infect Dis 2017;64:972-80.
7. Gutiérez-Gutiérrez B, Rodríguez-Bano J. Current options for the treatment of infections due to extended-spectrum beta-lactamase-producing Enterobacteriaceae in different groups of patients. Clin Microbiol Infect 2019;25:932-42.
8. Elder JS. Vesicoureteral reflux. In: Kliegman RM, Stanton BF, St. Geme JW III, Schor NF, Behrman RE, editors. Nelson textbook of pediatrics. 21st ed. Philadelphia (PA): Elsevier, 2019:2796-800.

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