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Meropenem/Vaborbactam in Pediatrics: 2 Cases of CRE Intraabdominal Infection

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Meropenem/vaborbactam is a combination antibiotic with a carbapenem and a carbapenemase inhibitor typically reserved for extensively drug-resistant bacterial infections, such as carbapenem-resistant Enterobacterales (CRE). Meropenem/vaborbactam is approved by the United States Food and Drug Administration for use in adults for complicated urinary tract infections, whereas data in the pediatric population are limited. This case series described the use of meropenem/vaborbactam in 2 pediatric patients, ages 11 and 15, with intraabdominal abscesses from CRE. Both patients had clinically improved after the initiation of meropenem/vaborbactam and reported no complications during their follow-up appointments after the completion of their antibiotic courses. These cases demonstrate the safe and effective use of meropenem/vaborbactam in these 2 pediatric patients. Although meropenem/vaborbactam successfully treated both patients' infections, additional data are needed in this population to determine the safety profile and optimal use for pediatric patients.

ABBREVIATIONS CRE, carbapenem-resistant Enterobacterales; IV, intravenous; KPC, *Klebsiella pneumoniae* carbapenemase.

KEYWORDS meropenem vaborbactam; intraabdominal infection; intraabdominal abscess; pediatric; case series.

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Introduction

Meropenem/vaborbactam gained its approval from the United States Food and Drug Administration in 2017 with an indication for the treatment of complicated urinary tract infections in adults. Meropenem is a carbapenem antibiotic that inhibits bacterial cell wall synthesis. Vaborbactam protects meropenem from being degraded by carbapenemases such as *Klebsiella pneumoniae* carbapenemase (KPC) via inhibition of these enzymes.[1] This antibiotic combination is typically reserved for extensively drug-resistant bacterial infections, such as carbapenem-resistant Enterobacterales (CRE).[2]

According to the Centers for Disease Control and Prevention, pediatric hospital-acquired infections associated with CRE species ranged from 0.5% to 3.7% between the years 2018 and 2021.[3–5] Common risk factors for CRE in the United States include exposure to intensive care units or contaminated medical equipment and previous treatment with antibiotics such as carbapenems and cephalosporins.[6] Many newer antibiotics have been developed to treat infections caused by these multidrug-resistant organisms; however, data in the pediatric population are limited at this time. We report 2 cases of the use of meropenem/vaborbactam in the treatment of CRE in pediatric patients.

Patient Case 1

An 11-year-old, 30-kg female presented to the emergency department for evaluation of a leaking surgical site with purulent, odorous discharge from her umbilical wound from a laparoscopic appendectomy performed 3 days prior. Her past medical history was significant for asthma. During her admission for the appendectomy, 3 doses of piperacillin/tazobactam 3.375 g (3 g per dose or 100 mg/kg/dose of the piperacillin component) intravenous (IV) every 6 hours infused over 30 minutes was administered empirically to the patient, with the last dose given 4 hours before surgery. After her procedure, she received acetaminophen and ibuprofen at home around the clock for pain. At home, the patient experienced a temperature of 102°F and some pain at the abdominal site. She had not had a bowel movement after discharge from the previous hospital stay despite using laxatives. On emergency department admission, she had an oral temperature of 98.1°F, a white blood cell count of 7.4 × 10^3/cmm, and a C-reactive protein of 0.56 mg/dL. An X-ray of the abdomen showed no indication of an infection.

On day 1, blood and superficial wound cultures were collected. An initial dose of vancomycin 600 mg (20 mg/kg) IV was given, followed by 450 mg (15 mg/kg/dose) IV every 6 hours. Additionally, piperacillin/

tazobactam 3.375 g (3 g per dose or 100 mg/kg/dose of the piperacillin component) IV every 8 hours infused over 30 minutes was administered. The patient was also prescribed acetaminophen for pain and fevers as needed. On day 2, she continued to experience pain, induration, and purulent drainage of the umbilicus wound. At this time, her white blood cell count and C-reactive protein remained normal. She was afebrile with a distended abdomen, so a sodium phosphate enema was administered.

On day 4, she had worsening pain at the surgical site with increased discharge. She was afebrile and experienced no leukocytosis. Her C-reactive protein was 0.38 mg/dL. The wound culture showed carbapenem-resistant *Escherichia coli* and *Bacteroides fragilis* (see Table). Owing to the resistance to carbapenem antibiotics, vancomycin and piperacillin/tazobactam were discontinued and ceftazidime/avibactam 1875 mg (1500 mg per dose or 50 mg/kg/dose of the ceftazidime component) IV every 8 hours infused over 2 hours was started empirically while additional susceptibility testing was conducted for ceftazidime/avibactam and meropenem/vaborbactam.

On day 5, the patient continued to be afebrile without leukocytosis, and she reported no pain at the umbilical surgical site with less purulent leakage present. Testing results indicated that the *E. coli* was susceptible to meropenem/vaborbactam and resistant to ceftazidime/avibactam (see Table). Ceftazidime/avibactam was then switched to meropenem/vaborbactam 2.4 g (1.2 g per dose or 40 mg/kg/dose of the meropenem component) IV every 8 hours, infused over 3 hours.

On day 6, the patient developed fecal stasis and continued to experience purulent leakage from the wound,

Table. Organism isolates and minimum inhibitor concentrations for patients 1 and 2.

	Patient 1		Patient 2	
Source	Abdominal Fluid		Abdominal Fluid	
Collection date	Day 1		Day 7	
Result Date	Day 4		Day 10	
Bacteria	*Escherichia coli*		*Enterobacter cloacae*	
Drug	MIC Interpretation	MIC Dilution	MIC Interpretation	MIC Dilution
Ampicillin	R	≥ 32		
Ampicillin-sulbactam	R	≥ 32		
Aztreonam	R	≥ 64	R	≥ 64
Cefepime	R	≥ 64	S	8
Ceftazidime	R	≥ 64	R	≥ 64
Ceftazidime-avibactam*	R*	256*	S†	1.5†
Ceftriaxone	R	≥ 64	R	≥ 64
Extended spectrum beta-lactamase	Negative	Negative		
Ertapenem			R	4
Gentamicin	S	≤ 1	S	≤ 1
Levofloxacin	R	≥ 8	S	≤ 0.12
Meropenem	R	≥ 16	S	1
Meropenem-vaborbactam*	S*	3*	S†	0.094†
Piperacillin/tazobactam	R	≥ 128		
Tobramycin	R	≥ 16	S	≤ 1
Trimethoprim-sulfamethoxazole	R	≥ 320	S	≤ 20

MIC, minimum inhibitory concentration
R, resistant
S, susceptible

* Result on day 5.
† Result on day 11.

though she denied any pain at this time. The meropenem/vaborbactam was continued until discharge for a total duration of 5 days and 10 total antibiotic days. By the time of discharge, the wound had a reduced amount of drainage with no erythema and less pain at the surgical incisions. Wound cultures were not reassessed. She continued to be afebrile. The treating team identified no adverse drug events on the clinical exam or routine labs. Her only discharge medication was polyethylene glycol 3350 17 g by mouth twice daily. She followed up with the infectious disease and surgery clinics a week after hospital discharge and appeared clinically improved without any complications.

Patient Case 2

A 15-year-old, 70.5-kg female with no significant past medical history presented to the emergency department with a 3-day history of new-onset lower abdominal pain associated with nausea and vomiting. She presented with a temperature of 98.3°F, a blood lactic acid of 0.7 mmol/L, and a white blood cell count of 7.4 × 10^3/cmm.

A computed tomography scan of the abdomen showed a closed-loop short bowel obstruction/volvulus. She underwent diagnostic laparoscopy and small bowel enterotomy on day 1 of admission. Before surgery, cefoxitin 2 g IV was administered. After the surgery, she received piperacillin/tazobactam 3.375 g (3 g per dose of the piperacillin component) IV every 6 hours, infused over 30 minutes, for a total of 5 days.

On day 7, the patient developed a fever of 102.2°F, and her serum procalcitonin was 61.82 ng/mL. She had been off antibiotics for 1 day when this occurred. She was tachycardic and hypotensive, which was managed with aggressive IV fluid resuscitation. The patient then developed generalized edema requiring IV serum albumin and IV furosemide. She was noted to have increased abdominal girth and pain. A repeat computed tomography scan of the abdomen and pelvis showed ascites and an abscess concerning bowel perforation. An exploratory laparotomy was performed, and cultures were obtained from the abdominal pelvic fluid and blood. She remained intubated postoperatively. Piperacillin/tazobactam 3.375 g (3 g per dose of the piperacillin component) IV every 6 hours infused over 30 minutes was restarted. She was also prescribed acetaminophen for pain and fevers as needed.

On day 10, the abdominal pelvic fluid culture results showed few (versus moderate or heavy—lab report descriptor terms) carbapenem-resistant *Enterobacter cloacae*, resistant to ertapenem and susceptible to meropenem (see Table). Additional susceptibilities for ceftazidime/avibactam and meropenem/vaborbactam were requested. Based on the susceptibility results, piperacillin/tazobactam (total duration of 3 days) was switched to meropenem IV 1 g every 8 hours, infused over 30 minutes. She was afebrile and remained intubated. Her procalcitonin serum concentration decreased to 19.23 ng/mL. On day 11, susceptibility results indicated that the *E. cloacae* was susceptible to ceftazidime/avibactam and meropenem/vaborbactam. At this time, she returned to the operating room for an abdominal washout and closure of the abdomen. Abdominal fluid was collected intraoperatively for culturing. On day 12, she experienced a fever of 101°F and a white blood cell count of 18 × 10^3/cmm. Prior white blood cell count measurements were within the normal range. The decision was made to switch meropenem (total duration of 3 days) to meropenem/vaborbactam 4 g (2 g per dose of the meropenem component) IV every 8 hours, infused over 3 hours. On day 13, she was extubated. The cultures continued to grow a few *E. cloacae* with similar resistance. Meropenem remained susceptible, and the combinations of ceftazidime/avibactam and meropenem/vaborbactam were not retested. She remained critically ill with intermittent fevers, requiring a higher level of care in the pediatric intensive care unit. The patient had 2 Jackson-Pratt drains and an open abdominal wound vacuum in place. Starting on day 23, she remained afebrile until discharge. On day 27, all drains and wound vacuums were removed. During this time, she was ambulating more frequently and required fewer pain medications for abdominal pain. She was transferred to the general pediatrics unit on day 30 and discharged on day 31.

At the time of discharge, the patient was afebrile, tolerating an oral diet without any nausea or vomiting, and had well-controlled pain. The final diagnosis was acute peritonitis, ileus, and intraabdominal abscess. Meropenem/vaborbactam was continued for an additional 2 weeks, for a total duration of 5 weeks, including the initial 5-day course of piperacillin/tazobactam. Antibiotic duration was determined based on the normalization of inflammatory markers. After discharge and throughout the course of meropenem/vaborbactam, she remained afebrile with occasional moments of abdominal pain but no issues with voiding or stooling. No adverse drug events were identified during the course of treatment. Once the antibiotic course was complete, she appeared well with no reported complications.

Discussion

We described 2 pediatric patients treated with meropenem/vaborbactam, an 11-year-old patient treated for carbapenem-resistant *E. coli* causing an intra-abdominal abscess, and a 15-year-old treated for carbapenem-resistant *E. cloacae* for acute peritonitis and intra-abdominal abscess. Both patients had clinically improved on discharge and reported no complications during their follow-up appointments after the completion of their antibiotic courses.

To our knowledge, past literature regarding the use of meropenem/vaborbactam monotherapy in pediatrics is limited to 2 case reports. The first case report

discussed a 4-year-old with *Klebsiella pneumoniae*-associated central-line–associated bacteremia.[7] This patient received meropenem/vaborbactam (meropenem component 40 mg/kg/dose) IV every 6 hours, infused over 3 hours, for 14 days. This regimen achieved targeted meropenem serum concentrations above the minimum inhibitory concentration and was associated with treatment success in this patient. The second case report discussed a 10-year-old patient with resistant *Achromobacter* spp-associated respiratory infection.[8] This patient received 2 courses of meropenem/vaborbactam, cefidercol, and bacteriophage therapy. During her second treatment course, she was administered meropenem/vaborbactam (2 g of the meropenem component) IV every 8 hours, infused over 3 hours, for 14 days. Based on cultures, the antibiotic combination appeared to be safe and effective in that pediatric patient. The value of meropenem/vaborbactam in the management of this patient's respiratory infection is unclear because additional treatments were provided simultaneously. Comparatively, our patients did not have a significant past medical history and only used 1 antibiotic at a time to manage their infections. Both of the case reports and our 2 cases infused meropenem/vaborbactam over 3 hours. The first case report dosed meropenem/vaborbactam every 6 hours while our patients improved clinically on a dosing strategy of every 8 hours. The increased frequency of dosing in the first case report may be due to the patient's younger age and critical illness. The authors concluded that this dosing strategy was associated with a successful bacteremia clearance in their pediatric patient. For reference, standard adult dosing is 4 g (2 g of the meropenem component) IV every 8 hours for a duration of 5 to 14 days. In our 2 cases, dose selection was based on the dose from the first case report with consideration to weight. The dose for our second patient was capped at the adult dose based on weight. A less frequent dosing strategy of meropenem/vaborbactam every 8 hours appeared to be sufficient for the treatment of intra-abdominal infections in both of our pediatric patients.

These cases also illustrate key antibiotic stewardship issues. For the first patient's case, her cultures grew *E. coli that* was susceptible to meropenem/vaborbactam but resistant to ceftazidime/avibactam despite having no previous exposure to ceftazidime/avibactam. Cases with discordant ceftazidime/avibactam and meropenem/vaborbactam susceptibilities have been reported, specifically due to KPC variants.[9,10] While genome sequencing to determine the specific mechanism of resistance was unavailable, the lower minimum inhibitory concentration of meropenem/vaborbactam compared with that of meropenem alone suggests this was also beta-lactamase mediated.

In our second patient's case, her cultures grew *E. cloacae*, which was susceptible to meropenem but resistant to ertapenem. Based on the Infectious Disease Society of America's guidelines for CRE infections in adults, the recommendation is to treat such cases with high-dose, extended-infusion meropenem.[2] In this case, the patient appeared to be clinically worsening while on meropenem and was therefore changed to meropenem/vaborbactam. Of note, the original dose of meropenem alone was 1 g IV every 8 hours infused over 30 minutes, while the meropenem/vaborbactam dose provided 2 g of the meropenem component, infused over 3 hours at the same dosing frequency. While the patient improved on meropenem/vaborbactam, it is unclear if this was due to the increased meropenem dose, the addition of vaborbactam, or both. From an antibiotic stewardship standpoint, there may have been an opportunity to avoid antibiotic escalation.[2] Without clear insight into the mechanism of resistance, escalation to meropenem/vaborbactam was the more reliable option.[2,11] Ultimately, these cases demonstrate that highly resistant Enterobacterales infections can occur in pediatric patients, even those with minimal prior antibiotic exposure. Prudent antibiotic use, which may require genomic testing and insights into resistance mechanisms, should be practiced to minimize the development of resistance.[9–11]

Of note, meropenem/vaborbactam is another combination antibiotic at risk for dosing errors in pediatrics due to the questionable convention of adult dosing based on the sum of components. Like piperacillin/tazobactam and ampicillin/sulbactam, the package insert recommends adult dosing as the sum of meropenem and vaborbactam (4 g, the sum of 2 g of meropenem and 2 g of vaborbactam). When clinicians then determine dosing in pediatrics, dosing is weight-based on the meropenem component alone. For our first patient, orders were entered based on the milligram per kilogram per dose of the beta-lactam component, while the doses for our second patient were entered as standard combined adult doses. This creates an opportunity for confusion when dosing based on a single component in pediatric patients. In our opinion, the ideal approach is dosing based on 1 component for adults and pediatrics to improve safety. Practitioners should use caution when ordering these medications for children.

Future Direction

Current ongoing research involving the use of meropenem/vaborbactam in pediatric patients includes the TANGO-KIDS trial.[12] This open-label, phase 3 study involves administering a single-dose infusion of meropenem/vaborbactam to determine dosing, pharmacokinetics, and safety in pediatric patients with serious bacterial infections. The estimated completion time for this study is set as June 2025. The data from this trial will provide greater insight into optimal dosing strategies for meropenem/vaborbactam in pediatric patients.

Conclusion

In this case series, meropenem/vaborbactam was associated with treatment success in carbapenem-resistant *E. coli*– and *E. cloacae*–associated intra-abdominal infections in 2 pediatrics patients. Both patients appeared to tolerate meropenem/vaborbactam without any noted adverse drug events. Additional published literature is needed in this population to determine the safety profile and optimal use for pediatric patients.

Article Information

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Ethical approval and informed consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation. All parents/caregiver(s) provided written informed consent and/or assent.

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References

1. Castanheira M, Huband MD, Mendes RE, et al. Meropenem-vaborbactam tested against contemporary gram-negative isolates collected worldwide during 2014, including carbapenem-resistant, KPC-producing, multidrug-resistant, and extensively drug-resistant enterobacteriaceae. *Antimicrob Agents Chemother*. 2017; 61(9):e00567–17.
2. Tamma PD, Aitken SL, Bonomo RA, et al. Infectious Diseases Society of America 2022 Guidance on the treatment of extended-spectrum β-lactamase producing enterobacterales (ESBL-E), carbapenem-resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with difficult-to-treat resistance (DTR-P. aeruginosa). *Clin Infect Dis.* 2022;75(2):187–212.
3. Centers for Disease Control and Prevention. Healthcare-associated infections: Table P8. Percent of CLABSI pathogens that were resistant to selected antimicrobials and classified as "urgent" or "serious" antimicrobial resistant threats, by location type, pediatrics, 2018-2021. Accessed September 13, 2023. https://www.cdc.gov/nhsn/hai-report/data-tables-pediatric/table-p8.html
4. Centers for Disease Control and Prevention. Healthcare-associated infections: Table P9. Percent of CAUTI pathogens that were resistant to selected antimicrobials and classified as "urgent" or "serious" antimicrobial resistant threats, pediatrics, 2018-2021. Accessed September 13, 2023. https://www.cdc.gov/nhsn/hai-report/data-tables-pediatric/table-p9.html
5. Centers for Disease Control and Prevention. Healthcare-associated infections: Table P10. Percent of SSI pathogens that were resistant to selected antimicrobials and classified as "urgent" or "serious" antimicrobial resistant threats for high-volume surgical categories, pediatrics, 2018-2021. Accessed September 13, 2023. https://www.cdc.gov/nhsn/hai-report/data-tables-pediatric/table-p10.html
6. Centers for Disease Control and Prevention. Healthcare-associated infections. Accessed February 4, 2024. https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html#:~:text=Healthcare%2Drelated%20risk%20factors%20include,cephalosporins%2C%20fluoroquinolones%2C%20and%20vancomycin
7. Hanretty AM, Kaur I, Evangelista AT, et al. Pharmacokinetics of the meropenem component of meropenem-vaborbactam in the treatment of KPC-producing Klebsiella pneumoniae bloodstream infection in a pediatric patient. *Pharmacotherapy*. 2018;38(12):e87–e91.
8. Gainey AB, Burch AK, Brownstein MJ, et al. Combining bacteriophages with cefiderocol and meropenem/vaborbactam to treat a pan-drug resistant Achromobacter species infection in a pediatric cystic fibrosis patient. *Pediatr Pulmonol*. 2020;55(11):2990–2994.
9. Shields RK, Chen L, Cheng S, et al. Emergence of ceftazidime-avibactam resistance due to plasmid-borne blaKPC-3 mutations during treatment of carbapenem-resistant Klebsiella pneumoniae infections. *Antimicrob Agents Chemother*. 2017:61:e02097–16.
10. Athans V, Neuner EA, Hassouna H, et al. Meropenem-vaborbactam as salvage therapy for ceftazidime-avibactam-resistant Klebsiella pneumoniae bacteremia and abscess in a liver transplant recipient. *Antimicrob Agents Chemother*. 2018:63:e01551–18.
11. Aurilio C, Sansone P, Barbarisi M, et al. Mechanisms of action of carbapenem resistance. *Antibiotics (Basel).* 2022;11(3):421.
12. Melinta Therapeutics, LLC. Dose-finding, pharmacokinetics, and safety of VABOMERE in pediatric subjects with bacterial infections (TANGOKIDS). ClinicalTrials.gov identifier: NCT02687906. Updated September 28, 2023. Accessed December 23, 2023. https://clinicaltrials.gov/study/NCT02687906#more-information