Extended-spectrum beta-lactamases (ESBL) producing *E. coli* are a common concern in daily practice. Carbapenems, especially ertapenem are the choice for the treatment in some hospitals, but aminoglycosides or trimethoprim and sulfamethoxazole are options for carbapenem saver. The aim of this study was comparing the clinical outputs in ESBL producing *E. coli* ITU in children treated with ertapenem or amikacin.

Methods. We designed a quasi-experimental study. In 2018 the antimicrobial stewardship program begins the use of amikacin for non-septic UTI for ESBL producing E. coli. Before this recommendation the use of ertapenem was common. We use WHONET 5.6 to identify ESBL producing *E. coli* UTI between 2016 and 2020. We analyzed the information using R 4.0.3.

Results. We analyzed 162 clinical records. 89 in ertapenem group, 45 in amikacin group, 23 in other treatments (TMP-SMX, meropenem) and 5 patients that received empirical treatment (Cefazolin) with clinical improvement and ambulatory management. The initial clinical and paraclinical variables was similar between two groups, only meropenem was more frequent in amikacin group as empiric treatment (table 1). Amikacin group received for media 7.4 days of antibiotic therapy (IQR 7-7.5) and ertapenem 8.2 days (IQR 7-10) (p value 0.049). The mortality, PICU requirement, mechanical ventilation and inotropic requirement was similar an both groups (Table 2). In amikacin group the median length of stay was 7.2 days (IQR 4-9) and in ertapenem group was 9 days (IQR 6-10). No significant adverse effects were documented in any group.

Table 1. Patient's characteristics in both groups.

	Ertapenem (89)	Amikacin (45)	p-value
Age months: median (IQR)	49,06 (10 – 53)	39.2 (9 – 53)	0.41
Sex			0.82
Masculine	20 (22,5%)	9 (20%)	
Feminine	69 (77,5%)	36 (80%)	
Type of infection			0.96
Asymptomatic bacteriuria	4(4.5%)	1(2.2%)	
Cystitis	8(9%)	4(8.8%)	
Pyelonephritis	76(85.3%)	39(86.6%)	
Urinary sepsis	1(1.1%)	1(2.2%)	
Urinary septic shock	0	0	
Empiric treatment			0,0006
Cefazolin	74(83.14%)	28(62.2%)	
Cefuroxime	2(2.2%)	3(6.6%)	
Meropenem	1(1.1%)	8(17.7%)	
Amikacin	3(3.3%)	3(6.6%)	
Ertapenem	6 (6.7%)	0	
Ceftriaxone	0	1(2.2%)	
Other	3(3.3%)	2(4.4%)	
Duration empiric treatment days. Median (IQR)	3 (2-3)	3 (2-3)	0.41
Prematurity			1
Yes	9 (10.1%)	5 (11.1%)	
No	71 (79.8%)	37 (82.2%)	
Missing	9 (10.1%)	3 (6.7%)	
Functional o anatomical disorder of urinary tract			0.38
Yes	23 (25.8%)	8 (17.8%)	
No	65 (73%)	37 (82.2%)	
Missing	1 (1.2%)		
Neurological disease			0.49
Yes	8 (9%)	2 (4.4%)	
No	81 (91%)	43 (95.6%)	
Missing	-	-	
First UTI			1
Yes	50 (56.2%)	26 (57.8%)	
No	39 (43.8%)	19 (42.2%)	
Missing	-	-	
Service			0.53
PICU			
Intermediate care unit	3(3.3%)	1(2.2%)	
General hospitalization	0	1(2.2%)	
Emergency room	86 (96.6%)	43 (95.5%)	

Table 2. Patient's Clinical outcomes in both groups

	Ertapenem (89)	Amikacin (45)	p-value
Duration of antibiotic days Median (IQR)	(IQR 7-10)	7.4 (IQR 7-7.5)	0.049
Change of etiological treatment			1
Yes	1 (1.1%)	0	
No	88 (98.9)	45 (100%)	
Missing			
Days of fever. Median (IQR)	3.2 (2-4)	4.5 (2-6)	0.17
Mechanical vent			1
Yes	0	0	
No	3(3.3%)	2(4.4%)	
Not PICU require	85(95.5%)	43(95.5%)	
Inotropic			1
Yes	0	0	
No	4 (4.5%)	1(2.2%)	
Not PICU require	5 (95.5%)	44(97.7%)	
Death			0.55
Yes	2(2.2%)	0	
No	87(97.7%)	45(100%)	
Length of stay in days. Median (IQR)	9 (6-10)	7.2 (4-9)	0.006
Antibiotic Side effects			1
Yes	0	0	
No	89 (100%)	45 (100%)	
Missing	-	-	
IVU Recurrent in 3 months			0.79
Yes	13 (14.6%)	7 (15.5%)	
No	71(79.7%)	32 (71.1%)	
Missing	5 (5.6%)	6 (13.3%)	

Conclusion. The use of amikacin in ESBL producing *E. coli* UTI in children have similar clinical outputs that ertapenem. The use of amikacin could decrease de hospitalization time.

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1154. Safety and Efficacy of Ceftolozane/Tazobactam Plus Metronidazole Versus Meropenem in Pediatric Participants With Complicated Intra-abdominal Infection: A Phase 2, Randomized Clinical Trial

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Session: P-64. Pediatric Bacterial Studies (natural history and therapeutic)

Background. Ceftolozane/tazobactam (C/T), a cephalosporin–β-lactamase inhibitor combination, is approved for treatment of complicated urinary tract infections, complicated intra-abdominal infections (cIAI), and nosocomial pneumonia in adults. Safety and efficacy of C/T in pediatric participants with cIAI was assessed.

Methods. This phase 2 study (NCT03217136) compared C/T + metronidazole (MTZ) with meropenem (MEM) for treatment of cIAI. Age- and weight-adjusted dosing is summarized in Table 1. The primary objective was to evaluate the safety and tolerability of C/T + MTZ compared with MEM. A key secondary endpoint was clinical cure at end of treatment (EOT) and test of cure (TOC).

Table 1. Summary of Dosing and Pharmacokinetic Sampling Schedule by Age Cohort

Table 1. Summary of Dosing and Pharmacokinetic Sampling Schedule by Age Cohort

Treatment	12 to <18 years (n=21)	6 to <12 years (n=39)	2 to <6 years (n=29)	3 months to <2 years (n=1)	Birth[a] to <3 months (n=1)
C/T + MTZ	Ceftolozane 1 g/ tazobactam 0.5 g + 10 mg/kg MTZ[b]	Ceftolozane 20 mg/kg / tazobactam 10 mg/kg[c] + 10 mg/kg MTZ[b]	Ceftolozane 20 mg/kg / tazobactam 10 mg/kg[c] + 10 mg/kg MTZ[b]	Ceftolozane 20 mg/kg / tazobactam 10 mg/kg[c] + 10 mg/kg MTZ[b]	Ceftolozane 20 mg/kg / tazobactam 10 mg/kg[c] + 10-15 mg/kg MTZ[d]
MEM + placebo	20 mg/kg	20 mg/kg	20 mg/kg	20 mg/kg	20 mg/kg
Dose frequency[e,f]	Every 8 hours	Every 8 hours	Every 8 hours	Every 8 hours	Every 8 hours[g]

C/T, ceftolozane/tazobactam; IV, intravenous; MEM, meropenem; MTZ, metronidazole.

[a]Birth was defined as >32 weeks gestational age and ≥7 days postnatal.

[b]Maximum dose was 1.5 g/day.

[c]Maximum dose was ceftolozane 1 g/tazobactam 0.5 g.

[d]Participants >28 days of age: MTZ 10 mg/kg every 8 hours (maximum dose 1.5 g/day). For participants ≤28 days of age, the suggested dosing regimen was as follows: Participants ≤28 days of age and ≤2 kg: MTZ 15 mg/kg loading dose, then 7.5 mg/kg/dose every 12 hours; participants ≤28 days of age and >2 kg: MTZ 15 mg/kg loading dose, then 10 mg/kg dose every 8 hours. However, other site-specific standard of care MTZ dosing was permitted at the investigator's discretion.

[e]Each dose of C/T or MTZ or MEM or placebo was administered as a 60-minute (±10 minutes) infusion. C/T + MTZ or MEM + placebo was to be dosed every 8 hours (±1 hour) after the previous infusion. The second IV dose had a ±4-hour window for dosing to facilitate adjustment of the dosing schedule (once every 8 hours) to be carried out throughout the dosing period.

[f]After receiving at least 9 doses of double-blind IV study treatment, participants could be switched to open-label, standard of care, oral step-down therapy at the investigator's discretion. The total duration of study treatment (IV only or IV + oral) was a minimum of 5 days and a maximum of 14 days.

[g]Participants 7-28 days of age who received MTZ with a frequency other than every 8 hours were required to receive placebo at the same frequency to maintain blinding.

Results. A total of 94 participants were randomized 3:1; 91 were treated with C/T + MTZ (n=70) or MEM (n=21) comprising the modified intent-to-treat (MITT) population. The clinically evaluable population included 78 participants at EOT (C/T + MTZ, n=59; MEM, n=19) and 77 participants at TOC (C/T + MTZ, n=58; MEM, n=19). The most common diagnosis and pathogen in the MITT population were complicated appendicitis (C/T + MTZ, 91.4%; MEM, 100%) and Escherichia coli (C/T + MTZ, 67.1%; MEM, 61.9%). The mean (SD) intravenous therapy/overall treatment duration was 6.4 (2.8)/9.3 (3.6) days and 5.8 (1.8)/9.0 (3.2) days for C/T + MTZ and MEM, respectively. In total, ≥1 adverse events (AE) occurred in 80.0% and 61.9% of participants receiving C/T + MTZ and MEM, respectively (Table 2), of which 18.6% and 14.3% were considered drug related. Serious AE occurred in 11.4% (8/70) and 0% (0/21) of participants receiving C/T + MTZ and MEM, respectively; none were considered drug related. No drug-related study drug discontinuations occurred. In the MITT population, rates of clinical cure for C/T + MTZ and MEM at EOT were 80.0% and 95.2%, and at TOC were 80.0% and 100%, respectively (Figure 1); 6 of the 14 failures for C/T + MTZ were indeterminate responses scored as endpoint failures per protocol. In the clinically evaluable (CE) population, rates of clinical cure for C/T + MTZ and MEM were 89.8% and 100% at EOT, and 89.7% and 100% at TOC, respectively (Figure 1).

Table 2. Adverse Events (All Participants as Treated Population)

	C/T + MTZ (N=70)	Meropenem (N=21)	Difference[a] (95% CI)
Participants with, n (%)			
≥1 AE	56 (80.0)	13 (61.9)	18.1 (−2.6 to 41.1)
No AE	14 (20.0)	8 (38.1)	−18.1 (−41.1 to 2.6)
Drug-related[b] AE	13 (18.6)	3 (14.3)	4.3 (−17.6 to 19.1)
Serious AE	8 (11.4)[c]	0	11.4 (−4.6 to 21.0)
Serious drug-related[b] AE	0	0	0.0 (−15.6 to 5.3)
Died	0	0	0.0 (−15.6 to 5.3)
Discontinued due to AE	2 (2.9)	0	2.9 (−12.9 to 9.9)
Discontinued due to drug-related[b] AE	0	0	0.0 (−15.6 to 5.3)
Discontinued due to serious AE	2 (2.9)	0	2.9 (−12.9 to 9.9)
Discontinued due to serious drug-related[b] AE	0	0	0.0 (−15.6 to 5.3)

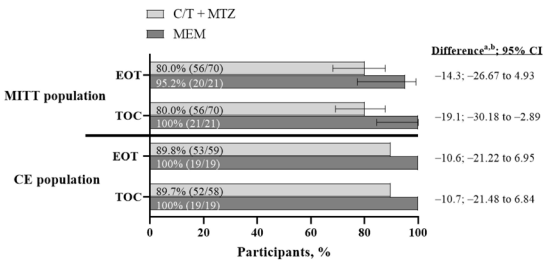
AE, adverse events; C/T, ceftolozane/tazobactam; MTZ, metronidazole.

[a] Difference in % (C/T + MTZ minus Meropenem) was based on the unstratified Miettinen & Nurminen method.

[b]Determined by the investigator to be related to the drug.

[c]Three of the serious AE in the C/T + MTZ group occurred during the intravenous treatment period (abdominal sepsis and pneumonia in 1 participant; intra-abdominal fluid collection in 1 participant) or during oral step-down therapy (fecaloma in 1 participant); all other serious AE were reported after study therapy was completed. All serious AE resolved.

Figure 1. Clinical Response in the MITT Population and Clinical Evaluable Populations at EOT and TOC



CE, clinically evaluable; C/T, ceftolozane/tazobactam; EOT, end of treatment; MEM, meropenem; MITT, modified intent-to-treat; MTZ, metronidazole; TOC, test of cure.

[a]Difference in ceftolozane/tazobactam + metronidazole minus meropenem.

[b]The percent difference was based on the Miettinen & Nurminen method stratified by age group with Cochran-Mantel-Haenszel weights. If there was a zero count in any class of the stratum, the groups with the lower count were pooled with the near age group stratum in the model.

Conclusion. C/T + MTZ was well tolerated in pediatric participants with cIAI, and rates of clinical success were high with C/T treatment. C/T is a promising new treatment option for children with cIAI.

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1155. Covering Your Tracts? The Effect of Antibiotic Prophylaxis on Respiratory Tract Infections in Pediatric Acute Lymphoblastic Leukemia

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Session: P-64. Pediatric Bacterial Studies (natural history and therapeutic)

Background. Antibiotic prophylaxis decreases rates of febrile neutropenia and systemic infection in children with acute lymphoblastic leukemia (ALL). However, it is unknown whether prophylaxis prevents or ameliorates the severity of specific types of infections like upper respiratory tract infections (URTI) or lower respiratory tract infections (LRTI).

Methods. This is a retrospective, observational convenience cohort study of children with newly-diagnosed ALL, comparing respiratory tract infections (RTI) in participants receiving no antibiotic prophylaxis, levofloxacin prophylaxis, or non-levofloxacin prophylaxis. Information regarding the presence of URTI or LRTI, identified respiratory viruses, hospitalization, oxygen supplementation, and ICU admission was collected through medical record review. The proportion of participants in each group was estimated and compared between groups using Fisher's exact test and the Kruskal-Wallis test.

Results. Of 262 evaluable participants, 126 received no antibiotic prophylaxis, 59 received levofloxacin prophylaxis, and 77 received non-levofloxacin prophylaxis, with a total of 136 children getting any antibiotic prophylaxis regimen. In the no-prophylaxis group, 22/126 (17.4%) had RTI, compared to 23/136 (16.9%) in the prophylaxis group. There was no significant difference in the numbers of LRTI and URTI, with or without an identified respiratory virus, regardless of the presence or type of antibiotic prophylaxis. Participants receiving prophylaxis did not have a significantly different risk of hospitalization, oxygen supplementation, or ICU admission.

Participant Characteristics

Characteristic	No prophylaxis (n=126)		Levofloxacin prophylaxis (n=59)		Other antibiotic prophylaxis (n=77)		P-value
	n	(%)	n	(%)	n	(%)	
Age, median (IQR), y	5.8	(3.5;11.9)	6.9	(3.8;11.8)	7.8	(3.8;12.1)	0.67
Age group							0.52
≥ 10 y	91	(72)	42	(71)	50	(65)	
< 10 y	35	(28)	17	(29)	27	(35)	
Sex							0.50
Male	77	(61)	36	(61)	41	(53)	
Female	49	(39)	23	(39)	36	(47)	
Race							0.57
White	97	(77)	48	(81)	65	(84)	
Black	21	(17)	10	(17)	9	(12)	
Others	8	(6)	1	(2)	3	(4)	
ALL risk category							0.003
Low	63	(50)	33	(56)	37	(48)	
Standard	63	(50)	23	(39)	32	(42)	
High	0	(0)	3	(5)	8	(10)	

Comparisons of levofloxacin prophylaxis, other prophylaxis, any prophylaxis, and no prophylaxis

Outcome	Relative Risk (95% CI)	P-value
Levofloxacin vs. no prophylaxis		
URTI	1.68 (0.81-3.47)	0.16
LRTI	0.53 (0.11-2.44)	0.41
Supplemental oxygen	6.35 (0.26-153.60)	0.26
Hospital admission for RTI	0.92 (0.45-1.87)	0.81
Other antibiotic vs. no prophylaxis		
URTI	0.70 (0.28-1.75)	0.45
LRTI	0.81 (0.25-2.63)	0.74
Supplemental oxygen	14.65 (0.80-268.50)	0.07
Hospital admission for RTI	0.62 (0.29-1.34)	0.23
Any prophylaxis vs. no prophylaxis		
URTI	1.13 (0.58-2.19)	0.73
LRTI	0.69 (0.25-1.95)	0.49
Supplemental oxygen	10.20 (0.57-182.57)	0.11
Hospital admission for RTI	0.75 (0.42-1.36)	0.34

URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection