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In Vitro Activity of Ceftolozane/Tazobactam against *Pseudomonas aeruginosa* from ICU and Non-ICU Patients with Respiratory Tract Infections in the Asia/Pacific region – SMART 2016-2018

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Introduction

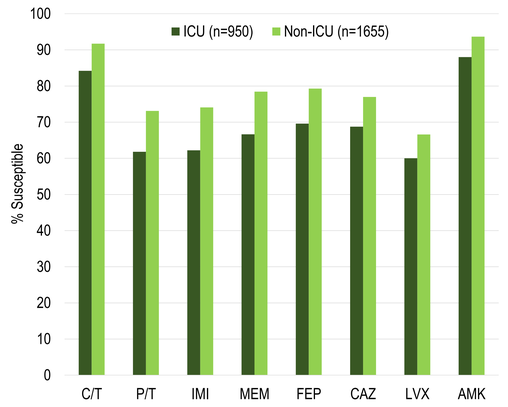
Ceftolozane/tazobactam (C/T) is an antipseudomonal cephalosporin combined with a β-lactamase inhibitor approved by FDA and EMA for hospital-acquired and ventilator-associated bacterial pneumonia. Elevated antimicrobial resistance rates have been reported among pathogens from patients in ICUs. Using isolates collected in Asia/Pacific as part of the Study for Monitoring Antimicrobial Resistance Trends (SMART) global surveillance program, we evaluated the activity of C/T and comparators against *P. aeruginosa* from patients with lower respiratory tract infections (RTI) in ICU and non-ICU wards.

Methods

In 2016-2018, 56 clinical laboratories in 11 Asia/Pacific countries collected 2,605 *P. aeruginosa* isolates from patients with RTI in ICU and non-ICU wards. MICs were determined using CLSI broth microdilution and interpreted with CLSI breakpoints [1, 2]. C/T-nonsusceptible isolates were screened by PCR and sequenced for genes encoding β-lactamases [3], except isolates collected from India (2016-2018), Vietnam (2017), one Vietnam site in 2018, and a small number of other isolates which were not available for molecular characterization and were not included in the denominators for carbapenemase rate calculations.

Results

Figure 1. Antimicrobial susceptibility of all *P. aeruginosa* isolates collected In Asia/Pacific, by ward type[a]



[a]Results for colistin are not shown because *P. aeruginosa* are no longer considered susceptible to colistin per 2020 CLSI guidelines.
C/T, ceftolozane/tazobactam; P/T, piperacillin/tazobactam; IMI, imipenem; MEM, meropenem; FEP, cefepime; CAZ, ceftazidime; LVX, levofloxacin; AMK, amikacin

Figure 2. Antimicrobial susceptibility of meropenem-nonsusceptible *P. aeruginosa* isolates, by ward type[a]

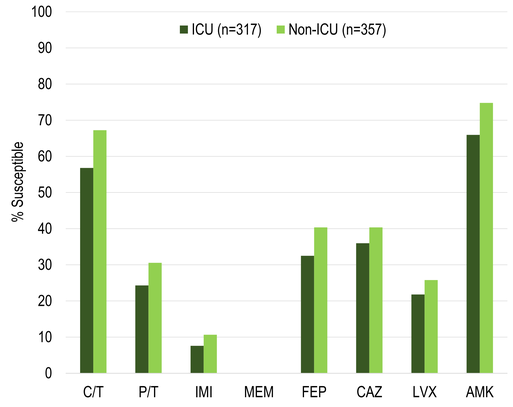


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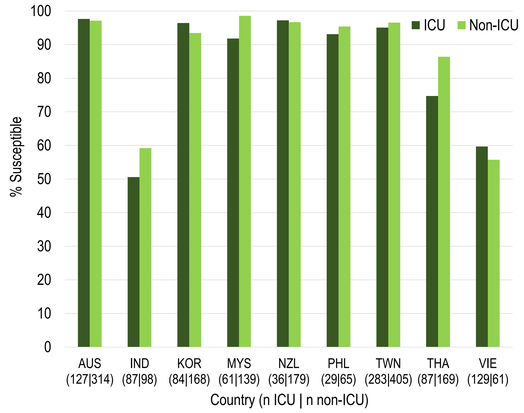
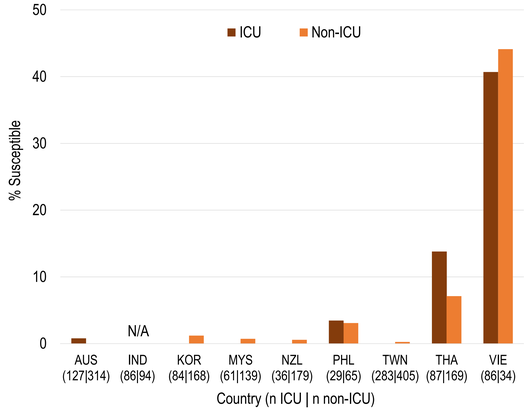
Figure 3. Antimicrobial susceptibility to C/T of all *P. aeruginosa* isolates, by country and ward type[a]



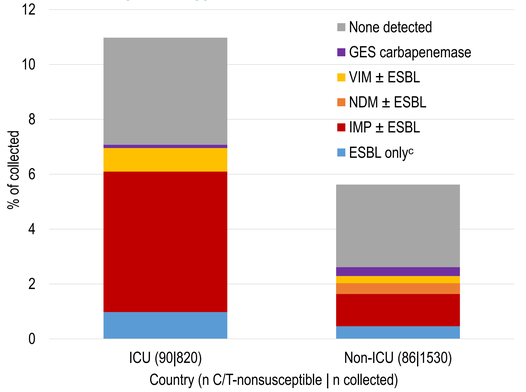
[a]Showing individually only countries with n>20 in both ICU and non-ICU subsets; not shown are Hong Kong and Singapore.
AUS, Australia; IND, India; KOR, South Korea; MYS, Malaysia; NZL, New Zealand; PHL, Philippines; TWN, Taiwan; THA, Thailand; VIE, Vietnam.

Figure 4. Proportion of carbapenemase-positive *P. aeruginosa* isolates, by country and ward type[a]



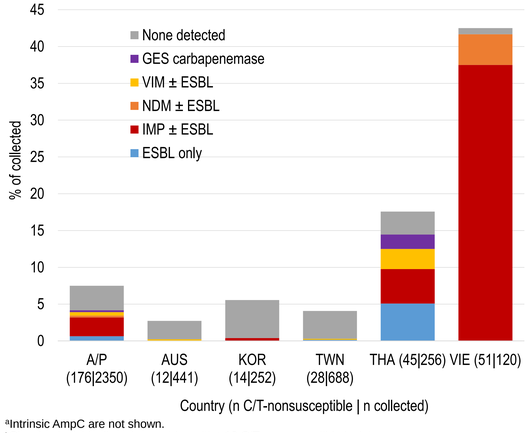
[a]Showing individually only countries with n>20 in both ICU and non-ICU subsets; not shown are Hong Kong and Singapore.
N/A, not available; AUS, Australia; IND, India; KOR, South Korea; MYS, Malaysia; NZL, New Zealand; PHL, Philippines; TWN, Taiwan; THA, Thailand; VIE, Vietnam.

Figure 5. Acquired β-lactamases detected in molecularly characterized C/T-nonsusceptible *P. aeruginosa* isolates from Asia/Pacific, by ward type[a]



[a]Intrinsic AmpC are not shown.
[c]Includes 5 VEB-positive, 2 GES-positive, and 1 SHV-positive isolate detected in ICUs and 7 VEB-positive isolates in non-ICU wards.
ESBL, extended-spectrum β-lactamase.

Figure 6. Acquired β-lactamases detected in molecularly characterized C/T-nonsusceptible *P. aeruginosa* isolates (ICU and non-ICU isolates combined), by country[a, b]



[a]Intrinsic AmpC are not shown.
[b]Showing individually only countries with >10 C/T-nonsusceptible isolates.
A/P, Asia/Pacific; AUS, Australia; KOR, South Korea; TWN, Taiwan; THA, Thailand; VIE, Vietnam; ESBL, extended-spectrum β-lactamase.

Results Summary

- Antimicrobial susceptibility was lower in ICUs than in non-ICU wards. Susceptibility to C/T was 84.2% in ICUs and 91.7% in non-ICU wards, 15-22 and 12-19 percentage points, respectively, higher than the tested comparator β-lactams (Figure 1).
- C/T maintained activity against 56.8% and 67.2% of meropenem-nonsusceptible isolates from ICU and non-ICU patients, respectively (Figure 2).
- At the country level, C/T susceptibility was not consistently lower among ICU than non-ICU isolates (Figure 3). Susceptibility to C/T was lowest for isolates collected in India, Vietnam, and Thailand, and >91% for the other countries.
- The high rates of carbapenemase-positive isolates observed for Thailand and Vietnam correlated inversely with C/T susceptibility (Figures 3 and 4).
- For Asia/Pacific overall, the proportion of carbapenemase-positive isolates was higher among C/T-nonsusceptible isolates from ICU than non-ICU wards (Figure 5). In both ward types, the majority of detected carbapenemases were metallo-β-lactamases (MBLs), with a substantially larger proportion of IMP-type MBLs among isolates collected from patients in ICU than non-ICU wards.
- The proportion of MBL-positive isolates was greatest among isolates collected in Vietnam (predominantly IMP-type) and Thailand (both IMP- and VIM-type). Additionally, 5 of 6 GES carbapenemases were found in isolates from Thailand (1 isolate was detected in New Zealand, not shown) (Figure 6).

Conclusions

In the Asia/Pacific region, C/T could provide an important treatment option for patients in both ICU and non-ICU wards with RTI caused by *P. aeruginosa*, especially in countries with low rates of carbapenemase-positive isolates.

References:

1. Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards – Eleventh Edition*. CLSI document M07-Ed11. 2018. CLSI, Wayne, PA.
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