EVALUATION OF THE IMPLEMENTATION AND IMPACT OF PIPERACILLIN-TAZOBACTAM PROLONGED INFUSIONS IN CRITICALLY ILL PATIENTS: A SINGLE-CENTER RETROSPECTIVE CHART REVIEW

critical care canada FORUM

AUTHORS

K. LANDRY[1,2], M. MACKENZIE[1,2], S BURGESS[2], P BONNAR[2], Y SHABI[2], G PATRIQUIN[2], V EICHHORN[2], K HOLLAND[2]

1 Dalhousie University, Halifax, Nova Scotia, Canada

2 Nova Scotia Health, Nova Scotia, Canada

CONTACT INFORMATION

Kylie Landry BSc(Pharm), ACPR

- Clinical Pharmacist, General Surgery
- Victoria General Hospital, QEII Health Sciences Centre
- 1276 South Park Street, Halifax, NS B3H 2Y9
- kylie.landry@nshealth.ca

ACKNOWLEDGEMENTS

Nova Scotia Health Central Zone Drug Use Evaluation Team

Nova Scotia Health Critical Care Database Team

INTRODUCTION

Altered pharmacokinetics in critically ill patients and increasing resistance makes antimicrobial dosing challenging [1-3]

Prolonged infusions of beta-lactams optimize pharmacokinetic/pharmacodynamic properties [1,2,4] and have been associated with decreased mortality [5]

In 2019, a prolonged piperacillin-tazobactam protocol was implemented at 2 Intensive Care Units (ICUs)

Dosing: A loading dose immediately followed by a dose appropriate for the patient's renal function infused over 6 hours every 6 hours

OBJECTIVES

Primary Objective:

- Describe and define the successful implementation of a prolonged piperacillin-tazobactam protocol

Secondary Objectives:

- ICU mortality and length of stay (LOS)
- Safety incidents
- Non-fermenting gram-negative bacilli (NF GNB) prevalence & minimum inhibitory concentrations (MICs) for piperacillin-tazobactam

METHOD

- Single-center retrospective observational study

Inclusion Criteria

- ≥ 16 years old
- Admitted to ICU between October 1, 2020, and October 1, 2022
- Received ≥ 2 doses of piperacillin-tazobactam

Exclusion Criteria

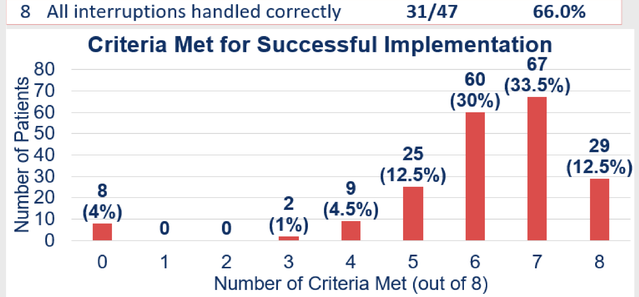
- Documentation of dose administration in the medication administration record (MAR) or nursing notes absent

- Convenience sample: 200 patients
- Successful implementation defined as meeting 6 of 8 predefined criteria
- Nova Scotia Health Research Ethics Board #1028843

RESULTS

Criteria for Successful Implementation

	Individual Criteria	Frequency	Percent
1	Order Set Used	180/200	90.0%
2	Initial Loading Dose	145/200	72.5%
3	Infusion started immediately after loading dose	45/145	31.0%
4	Dose appropriate for renal function	171/200	85.5%
5	Documentation in MAR q6h for bag change or infusion section for treatment duration	183/200	91.5%
6	If changed to intermittent infusion regimen started within 3 hours of stopping prolonged infusion	21/52	40.4%
7	No incompatible medications via same IV lumen	168/200	84.0%
8	All interruptions handled correctly	31/47	66.0%



ICU Mortality and LOS

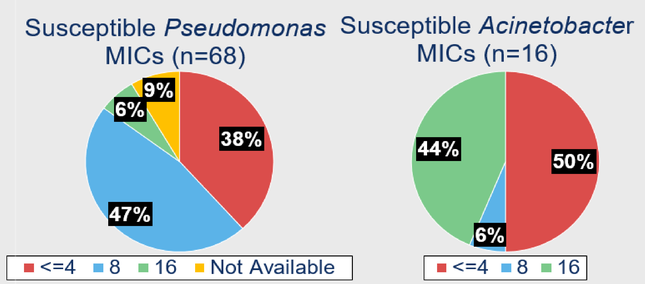
- 41/200 patients (20.5%) died in ICU
- 31/156 (19.9%) patients in the successful implementation and 10/44 (22.7%) in the unsuccessful implementation group died in ICU
- Median ICU LOS 4.9 days (IQR 2.4-10.7)

Safety Findings

- No safety incidents reported

Microbiologic Data

- Prevalence of NF GNB 3.1%



CONCLUSION

- Prolonged infusion protocol implemented successfully in 78% of the cohort
- No safety incidents reported
- Findings similar to prior studies:
  - Patients not on unit as a cause of interruptions in therapy (6)

Strengths	Limitations
Safety Data	Sample Size
Multi-disciplinary collaboration	Missing Data

- Areas for improvement have been identified and include editing the order set and interprofessional education and collaboration

REFERENCES

1. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017 Mar;43(3):304–77.
2. Guilhaumou R, Benaboud S, Bennis Y, Dahyot-Fizelier C, Dailly E, Gandia P, et al. Optimization of the treatment with beta-lactam antibiotics in critically ill patients—guidelines from the French Society of Pharmacology and Therapeutics (Société Française de Pharmacologie et Thérapeutique—SFPT) and the French Society of Anaesthesia and Intensive Care Medicine (Société Française d'Anesthésie et Réanimation—SFAR). Crit Care. 2019 Dec;23(1):104.
3. Yadav SK, Bhujel R, Mishra SK, Sharma S, Sherchand JB. Emergence of multidrug-resistant non-fermentative gram negative bacterial infection in hospitalized patients in a tertiary care center of Nepal. BMC Res Notes. 2020 Dec;13(1):319.
4. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clinical Infectious Diseases. 2016 Sep 1;63(5):e61–111.
5. Fawaz S, Barton S, Nabhani-Gebara S. Comparing clinical outcomes of piperacillin-tazobactam administration and dosage strategies in critically ill adult patients: a systematic review and meta-analysis. BMC Infect Dis. 2020 Dec;20(1):430.
6. Heinrich LS, Tokumaru S, Clark NM, Garofalo J, Paek JL, Grim SA. Development and Implementation of a Piperacillin-Tazobactam Extended Infusion Guideline. Journal of Pharmacy Practice. 2011 Dec;24(6):571–6.

INTRODUCTION

Altered pharmacokinetics in critically ill patients and increasing resistance makes antimicrobial dosing challenging [1-3]

Prolonged infusions of beta-lactams optimize pharmacokinetic/pharmacodynamic properties [1,2,4] and have been associated with decreased mortality [5]

In 2019, a prolonged piperacillin-tazobactam protocol was implemented at 2 Intensive Care Units (ICUs)

Dosing: A loading dose immediately followed by a dose appropriate for the patient’s renal function infused over 6 hours every 6 hours

OBJECTIVES

Primary Objective:

•Describe and define the successful implementation of a prolonged piperacillin-tazobactam protocol

Secondary Objectives:

•ICU mortality and length of stay (LOS)

•Safety incidents

•Non-fermenting gram-negative bacilli (NF GNB) prevalence & minimum inhibitory concentrations (MICs) for piperacillin-tazobactam

METHOD

- Single-center retrospective observational study

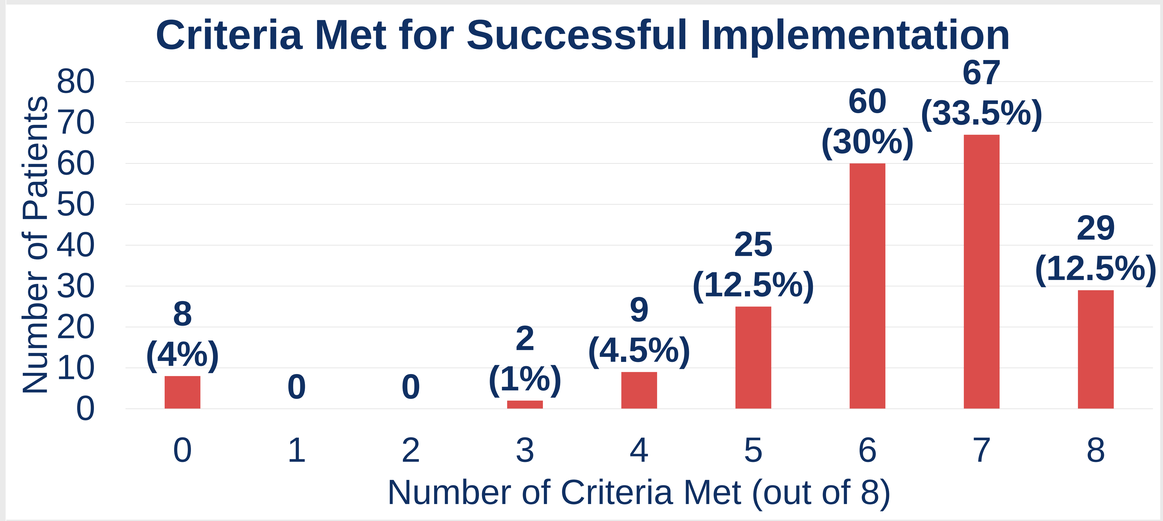
Inclusion Criteria	Exclusion Criteria
• ≥ 16 years old • Admitted to ICU between October 1, 2020, and October 1, 2022 • Received ≥ 2 doses of piperacillin-tazobactam	• Documentation of dose administration in the medication administration record (MAR) or nursing notes absent

- Convenience sample: 200 patients
- Successful implementation defined as meeting 6 of 8 predefined criteria
- Nova Scotia Health Research Ethics Board #1028843

RESULTS

Criteria for Successful Implementation

	Individual Criteria	Frequency	Percent
1	Order Set Used	**180/200**	**90.0%**
2	Initial Loading Dose	**145/200**	**72.5%**
3	Infusion started immediately after loading dose	**45/145**	**31.0%**
4	Dose appropriate for renal function	**171/200**	**85.5%**
5	Documentation in MAR q6h for bag change or infusion section for treatment duration	**183/200**	**91.5%**
6	If changed to intermittent infusion regimen started within 3 hours of stopping prolonged infusion	**21/52**	**40.4%**
7	No incompatible medications via same IV lumen	**168/200**	**84.0%**
8	All interruptions handled correctly	**31/47**	**66.0%**



ICU Mortality and LOS

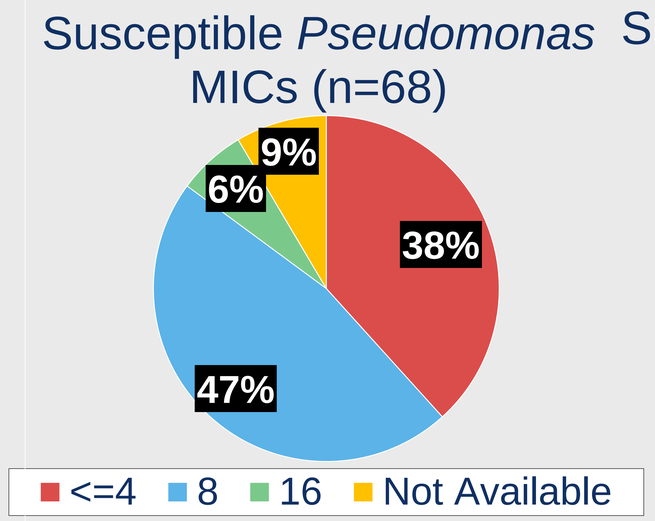
- 41/200 patients (20.5%) died in ICU
- 31/156 (19.9%) patients in the successful implementation and 10/44 (22.7%) in the unsuccessful implementation group died in ICU
- Median ICU LOS 4.9 days (IQR 2.4-10.7)

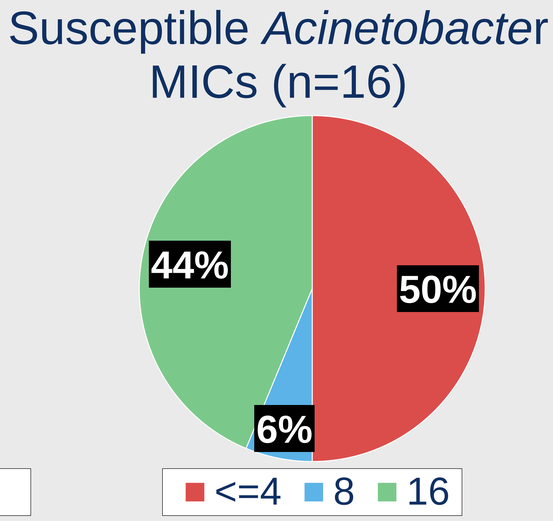
Safety Findings

- No safety incidents reported

Microbiologic Data

- Prevalence of NF GNB 3.1%





CONCLUSION

- Prolonged infusion protocol implemented successfully in 78% of the cohort
- No safety incidents reported
- Findings similar to prior studies:
  - Patients not on unit as a cause of interruptions in therapy (6)

Strengths	Limitations
Safety Data	Sample Size
Multi-disciplinary collaboration	Missing Data

- Areas for improvement have been identified and include editing the order set and interprofessional education and collaboration

ACKNOWLEDGEMENTS

Nova Scotia Health Central Zone Drug Use Evaluation Team

Nova Scotia Health Critical Care Database Team

Can be Vancouver style i.e. 1 Meyer J-P et al. The treatment of high grade superficial bladder cancer and carcinoma in situ with BCG – a questionnaire survey of Consultant practice in England and Wales. Urol Oncol 2002; 2;: 77-80

REFERENCES

1. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017 Mar;43(3):304–77.
2. Guilhaumou R, Benaboud S, Bennis Y, Dahyot-Fizelier C, Dailly E, Gandia P, et al. Optimization of the treatment with beta-lactam antibiotics in critically ill patients—guidelines from the French Society of Pharmacology and Therapeutics (Société Française de Pharmacologie et Thérapeutique—SFPT) and the French Society of Anaesthesia and Intensive Care Medicine (Société Française d'Anesthésie et Réanimation—SFAR). Crit Care. 2019 Dec;23(1):104.
3. Yadav SK, Bhujel R, Mishra SK, Sharma S, Sherchand JB. Emergence of multidrug-resistant non-fermentative gram negative bacterial infection in hospitalized patients in a tertiary care center of Nepal. BMC Res Notes. 2020 Dec;13(1):319.
4. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clinical Infectious Diseases. 2016 Sep 1;63(5):e61–111.
5. Fawaz S, Barton S, Nabhani-Gebara S. Comparing clinical outcomes of piperacillin-tazobactam administration and dosage strategies in critically ill adult patients: a systematic review and meta-analysis. BMC Infect Dis. 2020 Dec;20(1):430.
6. Heinrich LS, Tokumaru S, Clark NM, Garofalo J, Paek JL, Grim SA. Development and Implementation of a Piperacillin-Tazobactam Extended Infusion Guideline. Journal of Pharmacy Practice. 2011 Dec;24(6):571–6.

CONTACT INFORMATION

Kylie Landry BSc(Pharm), ACPR

- Clinical Pharmacist, General Surgery
- Victoria General Hospital, QEII Health Sciences Centre
- 1276 South Park Street, Halifax, NS B3H 2Y9
- kylie.landry@nshealth.ca

RESULTS

Demographics

Characteristic	Frequency n=200 (%)
Male	**118 (59.0%)**
Immunocompromised	**72 (36.0%)**
Mean Age (Years)	**59.6 (SD 16.3)**
Median APACHE IV Score	**38.7 (IQR 13.8 – 70.9)**
Median Duration of Piperacillin-Tazobactam Therapy (Days)	**1.98 (IQR 0.9 – 3.4)**

Loading Doses

- 26 patients who did not receive loading dose were not ordered one.
- 19/26 received piperacillin-tazobactam prior to ICU admission, a median of 5.0 hours (IQR 3.3-9.5) earlier

Interruptions