# Antimicrobial Stewardship (ASP) Evaluation of Meropenem Use at a Large Academic Medical Center

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## ABSTRACT (REVISED)

**Background:** Judicious carbapenem use in hospitalized patients is an important goal of an antimicrobial stewardship program (ASP). Use of meropenem, the formulary carbapenem at our University hospital, is restricted to the ASP, infectious diseases (ID), and critical care. We report an ASP initiative to assess meropenem utilization and prescribing patterns after a change in our ASP ordering process due to implementation of a new computerized order entry system (CPOE).

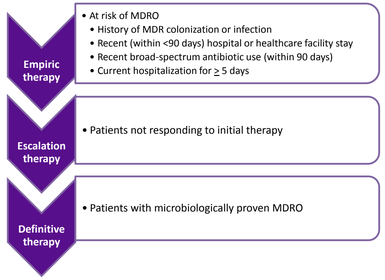
**Methods:** Meropenem utilization was measured in days of therapy (DOT)/1000 patient (pt) days. Microbiological data, clinical and treatment characteristics were evaluated retrospectively for all patients who received ≥1 dose of meropenem during 2nd quarter (Q2) of 2013. A gram-negative (GN) isolate was considered an MDRO if non-susceptible to ≥1 agent in ≥3 antimicrobial classes.

**Results:** In Q2 of 2013 as compared to Q2 of 2012 meropenem use increased by a mean of 62 DOT/1000 pt-days in intensive care units [ICU], p=0.18, and by 12 DOT/1000 pt-days in non-ICU units, p=0.31. Among 145 patients who received meropenem during Q2 of 2013, 43 were in ICU at meropenem start. Most common approval source was from ID attending (43%) followed by an approval from critical care (24%) and ASP team (21%). Positive cultures with GN organisms were present in 53% of patients, and 44% of these were MDRO. The most common site of positive culture was urine, followed by lungs and blood. Median duration of meropenem was 7 (range 1-37) days. In ICU, twice as many patients received >14 days of therapy vs. non-ICU (15.9% vs. 8.5%, p=0.27). Meropenem was used as escalation of therapy in 76% of patients (only 2/110 were due to discordant initial therapy). Escalation of therapy within ≤24h was twice as frequent in ICU vs. non-ICU (35% vs. 19%, p=0.1). Meropenem was deescalated in 18% of patients. An additional 22% of patients could have been deescalated based on susceptibility results. In logistic regression, prior MDRO infection or colonization (within 90 days) was identified as a predictor of current MDRO infection (OR 4.12, 95% CI 1.13-15.05, p=0.032) after adjusting for age >65 yrs, presence of comorbidities, need for ICU admission, and vasoactive agents at meropenem start.

**Conclusion:** ASP recommendations based on our findings include: implementation of CPOE flag for patients with prior MDRO; report meropenem quarterly utilization trends to ICU and ID attending; and we believe a collaborative agreement targeting initiation of restricted antibiotics and de-escalation by our ASP team is critical to improve appropriate meropenem utilization.

## BACKGROUND

- Judicious carbapenem use in hospitalized patients is an important goal of an antimicrobial stewardship program (ASP)
- According to our ASP guidelines for common infections, meropenem, the formulary carbapenem at our hospital, is reserved as:




- Due to broad spectrum of activity and high potential to cause collateral damage, meropenem is restricted to:
  - Antimicrobial Stewardship Program (ASP), Infectious Diseases (ID), and Critical Care (CC)

## OBJECTIVE

- To report an ASP initiative to assess meropenem utilization and prescribing patterns after change of ASP ordering process due to implementation of new computerized order entry system (CPOE)

## METHODS

**Study Design**
- Retrospective review of electronic medical records (EMR)

**Patients**
- Hospitalized adult (≥18 yrs) who received ≥ 1 dose of meropenem during 2nd quarter (Q2) of 2013 (April 1 – June 30)

**Data collection**
- Microbiological data, clinical and treatment characteristics

**Endpoints**
- Meropenem utilization in days of therapy (DOT)/1000-pt days
- Meropenem prescribing patterns
- Predictors of current MDRO

## RESULTS

| Table 1. Patient Characteristics | N=145 |
|---|---|
| Age, years, median (IQR) | 64 (54-75) |
| Male, sex | 73 (50) |
| Length of hospitalization, days, median (IQR) | 15 (8-24) |
| ICU stay, days, median (IQR) | 10 (5-13) |
| ID consult | 113 (78) |
| In-hospital mortality | 34 (23) |
| Withdrawal of care | 21 (62) |
| **Comorbidities** | |
| Malignancy | 52 (36) |
| Diabetes mellitus | 40 (28) |
| Transplant recipients | 14 (10) |
| Chronic kidney disease | 13 (9) |
| **Risk factors for MDRO** | |
| Prior hospitalization (90 days) | 68 (47) |
| Current hospitalization ≥ 5 days | 59 (41) |
| Antibiotic use prior to admission (90 days) | 62 (43) |
| Prior MDR colonization or infection (90 days) | 16 (11) |
| Resident of nursing home or LTCF | 6 (4) |
| At least 1 risk factor | 117 (81) |
| At least 2 risk factors | 65 (45) |
| **Characteristics at start of meropenem** | |
| WBC, cells/mm$^3$, median (IQR) | 14.4 (8.6-21.1) |
| Creatinine clearance, mL/min, median (IQR) | 42.1 (18.8-79.6) |
| ICU location | 63 (43) |

All values shown as n (%) unless otherwise specified, MDRO multi-drug resistant organism, ICU intensive care unit, ID infectious diseases, WBC white blood cell, IQR Interquartile range

## RESULTS (CONT.)

| Table 2. Microbiological Data | N=145 |
|---|---|
| Positive culture (GN organisms) | 77 (53) |
| Multi-drug resistant organisms | 34 (23) |
| *Enterobacteriaceae spp.* | 58 (75) |
| *Pseudomonas aeruginosa* | 16 (21) |
| *Stenotrophomonas maltophilia* | 5 (6) |
| *Acinetobacter baumanii* | 4 (5) |
| **Susceptibility**[1] | |
| *Enterobacteriaceae spp.* | n =70 |
| Cefepime | 60 (86) |
| Meropenem | 66 (84) |
| Piperacillin tazobactam | 55 (81) |
| Ciprofloxacin | 50 (63) |
| *P. aeruginosa* | n = 16 |
| Meropenem | 12 (75) |
| Cefepime | 12 (75) |
| Piperacillin tazobactam | 10 (62.5) |
| Ciprofloxacin | 10 (62.5) |
| *A. baumanii* | n = 4 |
| Ampicillin sulbactam | 3 (75) |
| Ciprofloxacin | 3 (75) |
| Meropenem | 2 (50) |
| Cefepime | 1 (25) |

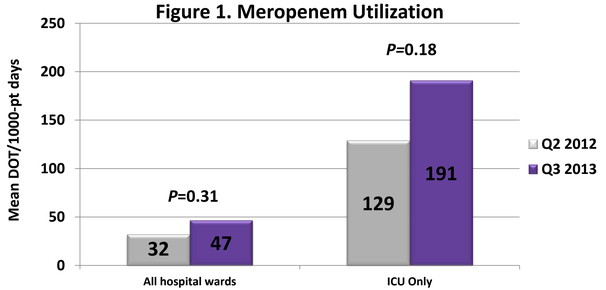
All values shown as n (%); [1] percent of susceptible isolates to specified antibiotic

**Table 3. Site of Infection in Patients with Positive Culture**

| Site | All patients (n=77) | ICU patients (n=28) | Non-ICU patients (n=49) |
|---|---|---|---|
| Urine | 40 (52) | 11 (39) | 29 (59) |
| Lung | 29 (38) | 14 (50 | 15 (31) |
| Blood | 23 (30) | 12 (43) | 11 (22) |
| SSTI | 8 (10) | 5 (18) | 3 (6) |
| IAI | 7 (9) | 2 (7) | 5 (10) |
| Other | 1 (1) | 0 | 1 (2) |

All values shown as (%), SSTI skin soft tissue infection, IAI Intra-abdominal infection

**Figure 1. Meropenem Utilization**




| Table 4. Details of Meropenem Treatment Course | All patients, N=145 | ICU patients, n=63 | Non-ICU patients, n=82 |
|---|---|---|---|
| Time to initiation since admission (days) | 5 (1,8) | 3 (1,6) | 3 (1,9) |
| Meropenem as initial therapy | 35 (24) | 11 (17.5) | 24 (29.3) |
| **Meropenem as escalation of therapy**[1,2] | **110 (76)** | **52 (82.5)** | **58 (70.7)** |
| Time to escalation <24 h[2] | 29 (26) | 18 (34.6)[3] | 11 (19) |
| Duration of therapy (days)[4] | 7 (4,11) | 7 (4,12) | 6.5 (4,11) |
| DOT >14 days[5] | 17 (11.7) | 10 (15.9) | 7 (8.5) |
| Discontinued within 24 h | 8 (6) | 4 (6.3) | 4 (4.9) |
| De-escalated | 26 (18) | 11 (17.5) | 15 (18.3) |
| By infectious diseases attending | 17/26 (65) | 10 | 7 |
| Was possible to deescalate based on cultures | 12/55 (22) | 5/20 (25) | 7/35 (20) |

All values shown as median (IQR) unless otherwise specified, [1] 2/110 due to discordant initial therapy, [2]$P$=0.1; [3]ICU patients 13 /18 (72%) on vasoactive agents, [4]Duration of therapy ≤ 1 day excluded, [5]$P$=0.27

**Figure 2. Approval Source**

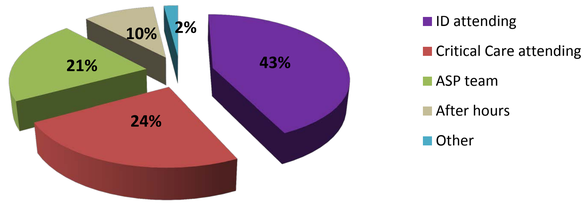



**Table 5. Predictors of Current Infection with MDRO**

| | Patients with MDRO, n=34 | Patients without MDRO, n=111 | Univariate analysis OR (95% CI) | Univariate analysis P-value | Multivariate analysis OR (95% CI) | Multivariate analysis P-value |
|---|---|---|---|---|---|---|
| Comorbidities | 17 (50) | 74 (66.7) | 0.5 (0.229-1.090) | 0.082 | 0.645 (0.264-0.578) | 0.7 |
| **Prior MDR infection or colonization** | **10 (29.4)** | **6 (5.4)** | **7.292 (2.415-22.015)** | **0.0005** | **4.116 (1.126-15.048)** | **0.032** |
| ≥3 MDRO risk factors | 11 (32.4) | 14 (12.6) | 3.314 (1.332-8.242) | **0.016** | 1.783 (0.583-5.454) | 0.311 |
| Pressors at meropenem start | 5 (14.7) | 41 (36.9) | 0.294 (0.106-0.820) | **0.01** | 0.414 (0.108-1.584) | 0.198 |
| ICU at meropenem start | 9 (26.5) | 54 (48.6) | 0.380 (0.163-0.887) | **0.02** | 0.645 (0.210-1.981) | 0.444 |
| Age >65 yrs | 18 (52.9) | 45 (40.5) | 1.650 (0.762-3.573) | 0.203 | 1.915 (0.797-4.597) | 0.146 |

## CONCLUSION

- In the Q2 of 2013 as compared to the Q2 of 2012, meropenem utilization increased in both ICU and non-ICU units, but did not reach statistical significance
- ASP recommendations based on our findings include:
  - Implementation of CPOE flag for patients with prior MDRO
  - Report meropenem quarterly utilization trends to ICU and ID attending
  - We believe a collaborative agreement targeting initiation of restricted antibiotics and de-escalation by our ASP team is critical to improve appropriate meropenem utilization

**Disclosure:** The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities.