ANTIMICROBIAL SUSCEPTIBILITY PATTERN COMPARISONS AMONG INTENSIVE CARE UNIT AND GENERAL WARD GRAM-NEGATIVE ISOLATES FROM THE MYSTIC PROGRAM (USA; 1999-2002)

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MYSTIC
Meropenem Yearly Susceptibility Test Information Collection

ABSTRACT

Background
The Meropenem Yearly Susceptibility Test Information Collection (MYSTIC) Program is a global, longitudinal antimicrobial surveillance of hospitals that prescribe meropenem [MEM]). The purpose of this investigation was to compare the prevalence of intensive care unit (ICU) to non-ICU pathogens, and assess differences in resistance (R) patterns between the two patient locations.

Methods
Fifteen medical centers submitted 200 isolates. Species with known intrinsic carbapenem-R patterns (methicillin-resistant *Staphylococcus aureus* [MRSA], *Enterococcus faecium*, *Stenotrophomonas maltophilia*) were excluded. National Committee for Clinical Laboratory Standards (NCCLS) susceptibility (S) testing methods were followed by a central laboratory. Results were sorted by ICU versus non-ICU hospital wards.

Results
A total of 5389 bacterial isolates were tested including 3884 Enterobacteriaceae (ENT; 542 ICU and 3342 non-ICU isolates) and 1505 non-fermentative Gram-negative bacilli (NF; 310 ICU and 1195 non-ICU). MEM was the most potent agent tested against ENT in both settings ($MIC_{50/90}$, 0.03/0.06 µg/mL). S rate order for ICU isolates was: MEM = IMP (99%) > cefepime (98) > gentamicin = tobramycin (TOB; 94) > ciprofloxacin (93) > ceftriaxone = piperacillin/tazobactam (P/T; 92) > aztreonam = ceftazidime (90). All antimicrobials had excellent activities for ENT in the non-ICU locations. MEM and TOB had the highest S rates for NF isolates in the non-ICU (88%) and ICU (82%). However, P/T had the least difference in S rates (80%) among isolates from either hospital location. Direct correlation (r=0.99) between those agents having higher S rates against ICU and non-ICU bacterial isolates was observed.

Conclusions
MEM continues to demonstrate the highest S rates against ENT within the non-ICU patient care areas and also against ENT within the ICU. None of the antimicrobials tested demonstrated high-level (≥ 90% coverage) against ICU NF. Longitudinal surveillance programs should continue to play an important role by providing therapeutic strategies for hospital environments with elevated broad-spectrum drug use and concentrations of at-risk patients.

INTRODUCTION

The Meropenem Yearly Susceptibility Test Information Collection (MYSTIC) Program is a global, longitudinal antimicrobial resistance surveillance study which began in 1997 and expanded in 1999 to include 15 United States (US) participant sites. Currently there are greater than 100 medical centers worldwide, each submitting data or bacterial isolates for central laboratory processing combined with antimicrobial usage statistics to correlate with microbiological resistance results.

This report compares the microbiological susceptibility and resistance rates of broad-spectrum antimicrobial agents against the Gram-negative strains isolated within intensive care units (ICUs) to those isolated from non-ICU patient locations. All information covers the entire MYSTIC Program data, processed by a central laboratory using National Committee for Clinical Laboratory Standards (NCCLS) reference methods.

Table 1. Activities and spectrum for activity of 11 antimicrobial agents tested against select Gram-negative bacterial isolates in ICUs and non-ICUs in the MYSTIC Program (1999-2002).

	ICU isolates (no. tested)				Non-ICU isolates (no. tested)			
Organism/antimicrobial agent	**MIC_{50}**	**MIC_{90}**	**%S**	**%R**	**MIC_{50}**	**MIC_{90}**	**%S**	**%R**
Enterobacteriaceae		(542)				(3342)		
Meropenem	0.03	0.06	98.7	1.1	0.03	0.06	99.9	0.1
Imipenem	0.25	2	98.7	1.1	0.25	2	99.7	0.1
Ceftriaxone	0.06	4	92.4	3.1	0.06	0.5	95.8	2.2
Ceftizoxime	0.06	4	91.4	6.5	0.06	1	94.3	3.8
Ceftazidime	0.25	16	89.7	8.1	≤0.12	1	94.8	4.2
Cefepime	≤0.12	0.5	98.0	1.5	≤0.12	0.25	99.4	0.4
Aztreonam	≤0.12	8	90.0	7.7	≤0.12	0.5	94.9	3.8
Piperacillin/Tazobactam	2	16	91.9	4.4	2	4	95.6	2.2
Gentamicin	≤2	≤2	93.5	5.4	≤2	≤2	95.4	3.6
Tobramycin	≤1	2	94.1	4.4	≤1	2	95.5	2.8
Ciprofloxacin	≤0.25	≤0.25	93.4	5.7	≤0.25	0.5	93.2	5.6
Non-fermentors		(310)				(1195)		
Meropenem	1	32	72.6	21.9	0.5	8	87.9	7.8
Imipenem	2	16	75.2	19.7	1	8	84.9	9.5
Ceftriaxone	>32	>32	12.9	65.8	>32	>32	18.3	57.6
Ceftizoxime	>32	>32	10.2	78.0	>32	>32	13.6	72.1
Ceftazidime	4	>16	73.2	20.6	4	>16	83.5	11.8
Cefepime	8	>16	67.1	18.4	4	16	80.3	9.0
Aztreonam	16	>16	43.2	44.2	8	>16	56.3	29.1
Piperacillin/Tazobactam	8	>128	80.0	20.0	8	64	90.2	6.1
Gentamicin	≤2	>8	69.7	22.6	≤2	>8	79.5	15.1
Tobramycin	≤1	>8	81.6	15.5	≤1	>8	85.4	12.9
Ciprofloxacin	0.5	>2	63.9	30.6	≤0.25	>2	71.9	22.4

MATERIALS AND METHODS

- Between 1999 and 2002, bacterial isolates were collected in 15 US participant medical centers (only 10 in 1999) and submitted to a central processing laboratory (JMI Laboratories, North Liberty, IA). Each medical center was requested to send up to 100 aerobic Gram-negative and 100 aerobic Gram-positive isolates from specified species with associated demographic data. *Stenotrophomonas maltophilia, Enterococcus faecium* and methicillin-resistant staphylococci isolates were excluded due to the known intrinsic resistance mechanisms to carbapenems.
- Over the 4-year study period, a total of 852 Gram-negative isolates were submitted from ICU patients and 4537 strains from other patient care areas. Susceptibility testing was performed using commercial, validated dry-form broth microdilution panels (TREK Diagnostics, Cleveland, OH). The core group of antimicrobial agents included: meropenem, imipenem, ceftriaxone, ceftizoxime, ceftazidime, cefepime, aztreonam, piperacillin/tazobactam, gentamicin, tobramycin and ciprofloxacin.
- Susceptibility and resistance was interpreted using current National Committee for Clinical Laboratory Standards [NCCLS, 2003] susceptibility testing methods (M7-A6) and interpretative criteria (M100-S13).

RESULTS

- Meropenem and imipenem demonstrated the highest activity as defined by the percentage of organisms inhibited at or below NCCLS breakpoints (> 98.7% susceptible) against the Enterobacteriaceae tested from both ICU and non-ICU care areas (Table 1).
- Several β-lactam antimicrobial agents demonstrated increases in the MIC_{90} results of 4- to 16-fold for the ICU Enterobacteriaceae isolates (Table 1).
- Tobramycin, piperacillin/tazobactam and the carbapenems exhibited the highest percent susceptibility against the non-fermentative Gram-negative bacilli in both the ICU and non-ICU organism populations (Table 1).
- Against the Enterobacteriaceae isolates tested, all 11 antimicrobial agents showed a lower percent susceptible and higher percentage resistance in the ICU compared to non-ICU care areas. Only ciprofloxacin susceptibility was nearly identical between monitored care areas (Table 1 and Figure 1).
- The ICU derived 'non-fermentor' isolates showed higher percent resistance rates (Figure 2) and lower percent susceptibility rates for all tested antimicrobial agents when compared to the non-ICU surveillance isolates.

Figure 1. Comparison of ICU and non-ICU resistance rates for the 11 monitored antimicrobials tested against the Enterobacteriaceae.

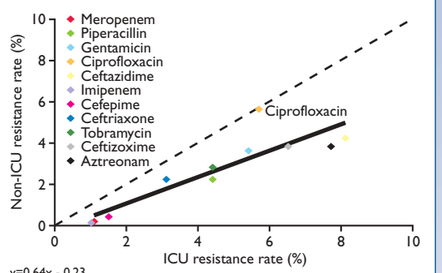


Figure 2. Comparison of ICU and non-ICU resistance rates for the 11 monitored antimicrobials tested against non-fermentative Gram-negative bacilli.

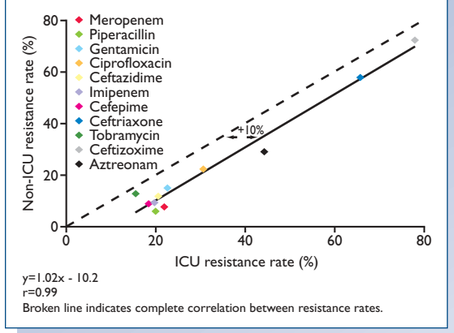
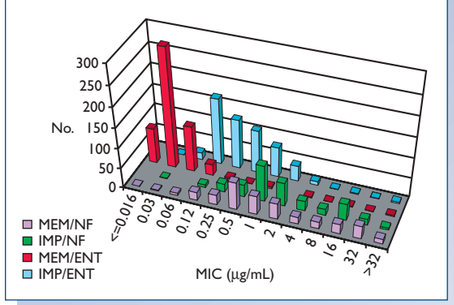


Figure 3. MIC population distributions for meropenem (MEM) and imipenem (IMP) tested against MYSTIC Program ICU isolates of Enterobacteriaceae (ENT) and non-fermentative Gram-negative bacilli (NF).



- Imipenem was consistently 2- to 4-fold less active when compared to meropenem against all tested organism populations especially ICU strains (Figure 3).
- Carbapenems, cefepime, piperacillin/tazobactam and tobramycin were the most valuable agents overall for therapy of ICU infections based on susceptibility rates (Table 1).

CONCLUSIONS

- **Meropenem and imipenem remain the most active broad-spectrum β-lactam antimicrobial agents against Gram-negative bacilli isolated in ICU or non-ICU patients.**
- **The MYSTIC Program isolates collected from participant medical centers demonstrated increased resistance rates for Enterobacteriaceae and non-fermentative bacilli isolated from patients within ICU compared to other patient care areas. Only the monitored fluoroquinolone (ciprofloxacin) showed no significant difference between organism populations, reflecting the wider selection toward resistance within both hospital and ambulatory care settings.**

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