Reduced Carbapenem Susceptibility in the Bacteroides fragilis Group – Findings from the TEST Program 2007-2010

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P1208

Revised Abstract

Background: Bacteroides fragilis group organisms are important anaerobic co-pathogens in many polymicrobial infections. Reduced susceptibility to carbapenems in B. fragilis group is due primarily to the beta-lactama-lactamase CIIA gene (meropenem MICs 1-4 μg/mL with high-level resistance secondary to acquired upstream insertion sequences (IS) causing expression of OXA (MICs ≥16). Methods: The Tigecycline European Surveillance Trial (TEST) evaluated 154/1842 (8.4%) B. fragilis group organisms with reduced susceptibility to carbapenems (meropenem MIC ≤3 μg/mL) from a collection of anerobes spanning four years, 2007-2010. The isolates were identified to the species level at the participating sites and confirmed by a central laboratory. MICs were determined by the central laboratory using agar dilution according to CLSI guidelines. Results: MICs of % susceptible of B. fragilis group with meropenem MICs ≤1 mg/mL by year (n= total B. fragilis group isolates):

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<th>2007</th>
<th>2008</th>
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Conclusions: B. fragilis group isolates with reduced susceptibility to meropenem increased significantly between 2007-2010 (p<0.05, Fisher’s exact test). Greater than 92% of these isolates were susceptible to tigecycline and metronidazole, with no significant reduction in susceptibility for any of the compounds tested over the four years of analysis.

Introduction

Susceptibility patterns of anaerobes have become less predictable owing to increasing antibacterial resistance. Emergence of highly virulent or multi-drug-resistant strains is further challenging current therapies. To counteract these trends, regular resistance surveillance in anaerobes, rational antibiotic use and evaluation of new treatment alternatives are important. Management of anaerobic infections encompasses surgical procedures, antibacterial therapy and adjuncts. At present, metronidazole, piperacillin-tazobactam, and beta-lactam/beta-lactamase inhibitor combinations exhibit the most promising activity though reports of increasing resistance to these agents are emerging (1). Recent data from the the Tigecycline Evaluation and Surveillance Trial (TEST) has shown that in addition to the above agents, tigecycline also exhibits promising activity and high susceptibilities against a wide range of anaerobes (2). The current study describes data from TEST, from 2007 to 2010, based on the activity of tigecycline and comparators against 1,842 isolates of Bacteroides spp. clinical isolates from various infection sources.

Materials & Methods

Clinical isolates: A total of 1,842 clinical isolates of Bacteroides spp. were collected during 2007-2010. Isolates were identified to the species level and tested at each participating laboratory. All organisms were deemed clinically significant by local participating criteria. Isolate inclusion was independent of medical history, antimicrobial use, age or gender. All sites identified each study isolate utilizing local laboratory criteria. All isolates were from the period 2007 - 2010 and originated from various infection sources and loc sites.

Susceptibility testing: All isolates were sent to a single reference laboratory for evaluation. Minimum inhibitory concentrations (MICs) were determined by agar dilution as specified by the Clinical and Laboratory Standards Institute (CLSI) (3) Susceptibility was determined using clinical breakpoints published by EUCAST (4).

Results

Figure 1. Distribution of all isolates (n = 1,842) by location.

Figure 5. Percent of all isolates (n = 1,842) and isolates with meropenem MICs ≥1 mg/L (n = 154) by infection source.

Figure 2. Distribution of isolates with meropenem MICs ≥1 mg/L (n = 154) by location.

Figure 6. Percent susceptibility of isolates with meropenem MICs ≥1 mg/L (n = 154) to tigecycline and comparators from 2007 – 2010.

Figure 3. Percent of all isolates (n = 1,842) and isolates with meropenem MICs ≥1 mg/L (n = 154) by location.

Figure 7. Percent susceptibility of isolates with meropenem MICs ≥1 mg/L (n = 154) to tigecycline and comparators from 2007 – 2010.

Figure 4. Distribution of all isolates (n = 1,842) and isolates with meropenem MICs ≥1 mg/L (n = 154) by infection source.

Conclusions

- Of the total of 1,842 clinical isolates collected from 2007 – 2010, 154 (8.4%) had meropenem MICs ≥1 mg/L, the majority of all isolates and isolates with meropenem MICs ≥ mg/L were from inpatient hospital locations
- The 1,842 isolates were most commonly isolated from skin and skin structure infections (51%) followed by gastrointestinal infection (25%). Isolates with meropenem MICs ≥1 mg/L were almost most commonly isolated from these sources (47% and 21%, respectively).
- Analysis of susceptibility to all isolates for all years of the study showed that percent susceptibility to tigecycline, metronidazole, piperacillin-tazobactam and meropenem remained ≥90% however decreases during the study period were noted for meropenem (98% in 2007 to 94% in 2010).
- Against isolates with meropenem MICs ≥1 mg/L, only tigecycline and metronidazole exhibited percent susceptibility of ≥90% for the whole study period.

References

Acknowledgements

We gratefully acknowledge the contributions of the investigators, laboratory personnel, and all members of the Tigecycline European Study Trial program. This study was sponsored by Pfizer, Inc.