

Revised Abstract

Background: The incidence of multi-drug resistant (MDR) *Clostridium* spp. is unclear. Surveillance studies aimed at determining their incidence and susceptibility to antibiotics are necessary in order to better understand the incidence of such etiologic agents. This study evaluated the activity of tigecycline and comparators against MDR *Clostridium* spp. isolated from nosocomial infections during 2007 - 2008. **Methods:** During the T.E.S.T surveillance study, *Clostridium* spp. were collected from hospitals in Europe. A cumulative total of 31 sites were involved from Belgium, Czech Republic, France, Germany, Hungary and the United Kingdom. Of a total of 546 isolates, 128 (23.4%) of these were designated as MDR (resistant to at least two antibiotics classes). Minimum Inhibitory Concentrations (MICs) were determined using agar dilution and interpreted according to CLSI breakpoints. **Results:** Results of tigecycline data from this study are shown in the following Table.

Year	Total Isolates	MDR (%)	MDR (% MDR) ^a	MIC ₉₀	% Susc ^b
2007	304	59	-19.4	0.5	100
2008	242	69	-28.5	0.12	100

^aNumber of MDR isolates and percent of isolates classified as MDR; ^bPercent of MDR isolates susceptible to tigecycline.

Conclusions: From a total of 546 isolates of *Clostridia*, 23.4% were MDR. Although the numbers of MDR *Clostridia* per year were relatively small, it appears that a transient increase in their incidence has occurred during the period 2007 – 2008. All MDR isolates were susceptible to tigecycline. Further monitoring of MDR *Clostridia* and their susceptibility to tigecycline is warranted.

Introduction

Clostridium spp., especially *C. difficile*, comprise the major causative pathogens of nosocomial gastrointestinal disorders [1] and in the case of *C. difficile* have been associated with causing large outbreaks of infection including the emergence of “hyper-virulent” strains [2]. Tigecycline is approved in the United States for the treatment of complicated skin and skin structure infections (cSSSI), complicated intra-abdominal infections (cIAI), and recently approved for the treatment of community acquired bacteria pneumonia (CABP), including pneumococcal bacteremia. Although FDA approved for several indications including the treatment of *Clostridium perfringens* in cIAI infection, the full prescribing information does not include the use of tigecycline for the treatment of infections due to *C. difficile* nor does it report *C. difficile* as an agent susceptible to the drug, nevertheless, tigecycline does support an FDA susceptible breakpoint for anaerobes of ≤4 mcg/ml [3]. As part of the ongoing global Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) program, the current study was designed to evaluate the *in vitro* activity of tigecycline and comparator antimicrobials against multi-drug resistant (MDR) isolates of *Clostridium* spp., collected from hospitals in Europe during 2007 – 2008.

Materials & Methods

Clinical isolates were collected during 2007-2008 from 31 hospital centers from 6 countries (Belgium, Czech Republic, France, Germany, Hungary, and United Kingdom). Only one isolate per patient was accepted. Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended agar dilution testing method [4]. Tigecycline was supplied by Wyeth Pharmaceuticals (Collegeville, PA, USA) and tested with clindamycin, metronidazole, piperacillin-tazobactam, meropenem and penicillin as comparators. MIC interpretive criteria followed published breakpoints established by Clinical and Laboratory Standards Institute (CLSI) and the FDA (tigecycline) [3, 4].

References

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Results

Table 1. Number of investigator sites by year and by country.

Country	2007	2008	Cumulative Total
Belgium	1	1	2
Czech Republic	1	1	2
France	5	4	9
Germany	7	5	12
Hungary	3	1	4
United Kingdom	0	1	1
Totals	17	13	30

Table 2. Source of organisms by *Clostridium* species collectively and Multi-Drug Resistant species.

All <i>Clostridium</i> spp			
Source	2007	2008	Grand Total
Blood	17	22	39
Catheters/Drains	1	0	1
Gastrointestinal	171	78	249
Genital/Urinary	4	0	4
Other	65	116	181
Respiratory	6	0	6
Skin and Skin Structures	40	26	66
Grand Total	304	242	546

MDR <i>Clostridium</i> Sources			
Source	2007	2008	Grand Total
Blood	1	1	2
Gastrointestinal	50	21	71
Other	3	46	49
Respiratory	1	0	1
Skin and Skin Structures	4	1	5
Grand Total	59	69	128

Table 3. Numbers and percentage of all *Clostridium* isolates and MDR *Clostridium* spp.

Organism	N	% N	MDR N	% MDR N
<i>Clostridium bifementans</i>	8	1.5	1	0.8
<i>Clostridium butyricum</i>	15	2.7	1	0.8
<i>Clostridium cadaveris</i>	3	0.5	0	0
<i>Clostridium clostridioforme</i>	21	3.8	3	2.3
<i>Clostridium difficile</i>	254	46.5	112	87.5
<i>Clostridium glycolicum</i>	2	0.4	0	0
<i>Clostridium hastiforme</i>	1	0.2	1	0.8
<i>Clostridium histolyticum</i>	4	0.7	0	0
<i>Clostridium innocuum</i>	13	2.4	1	0.8
<i>Clostridium novyi</i>	1	0.2	0	0
<i>Clostridium paraputrificum</i>	7	1.3	0	0
<i>Clostridium perfringens</i>	152	27.8	3	2.3
<i>Clostridium putrificum</i>	1	0.2	0	0
<i>Clostridium ramosum</i>	8	1.5	0	0
<i>Clostridium scatologenes</i>	2	0.4	0	0
<i>Clostridium septicum</i>	6	1.1	0	0
<i>Clostridium sordellii</i>	9	1.6	0	0
<i>Clostridium sphenoides</i>	1	0.2	1	0.8
<i>Clostridium sporogenes</i>	22	4.0	0	0
<i>Clostridium subterminale</i>	2	0.4	0	0
<i>Clostridium symbiosum</i>	1	0.2	0	0
<i>Clostridium tertium</i>	8	1.5	5	3.9
<i>Clostridium, non-specified</i>	5	0.9	0	0
Grand Total	546	100	128	100

N = Number isolated; % N = percent of all isolates; MDR N, number of MDR isolates; % MDR N, percent of isolates defined as MDR.

Figure 1. Activity of tigecycline and comparators against 128 MDR *Clostridium* isolates by MIC₉₀ (mcg/ml).

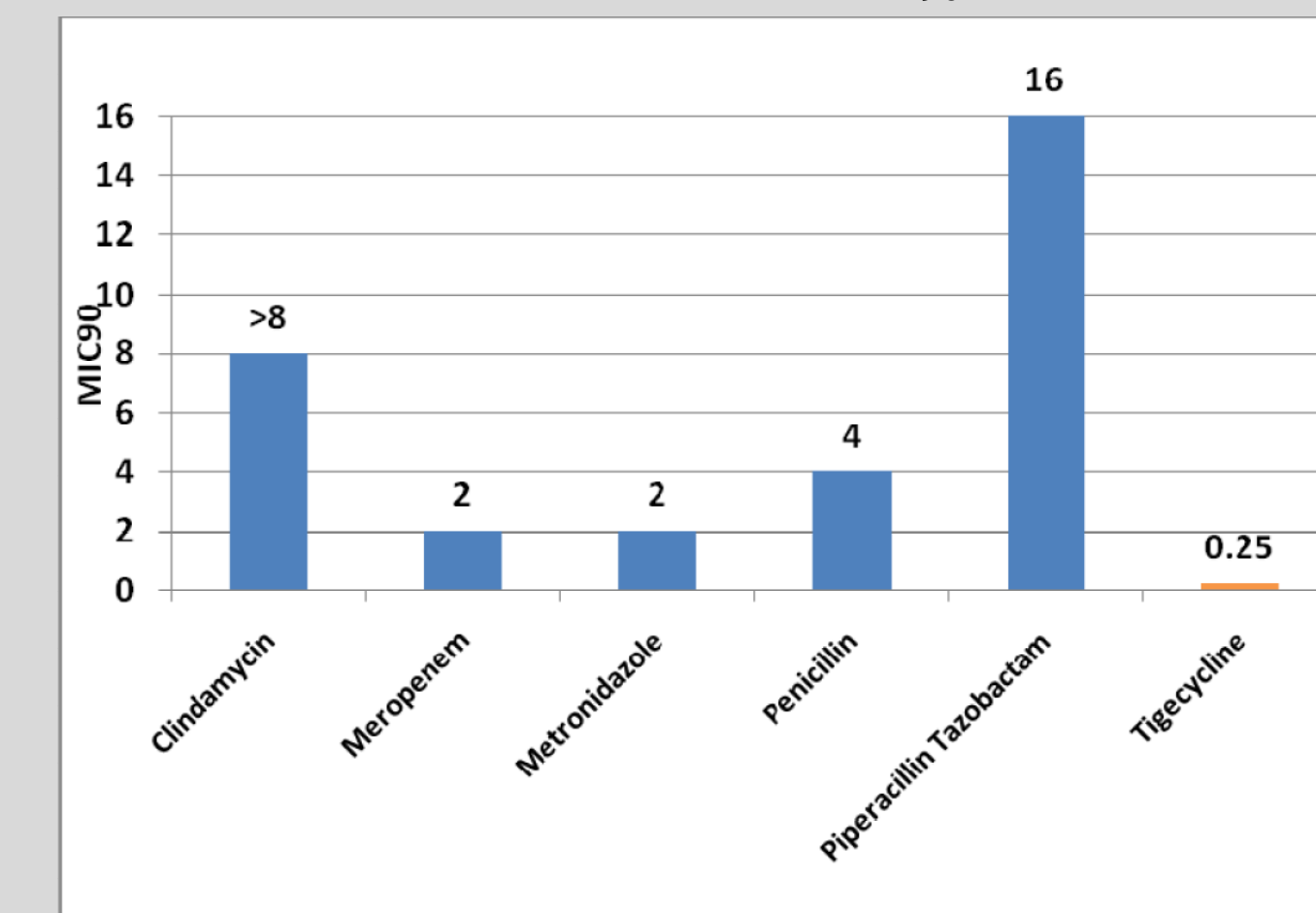
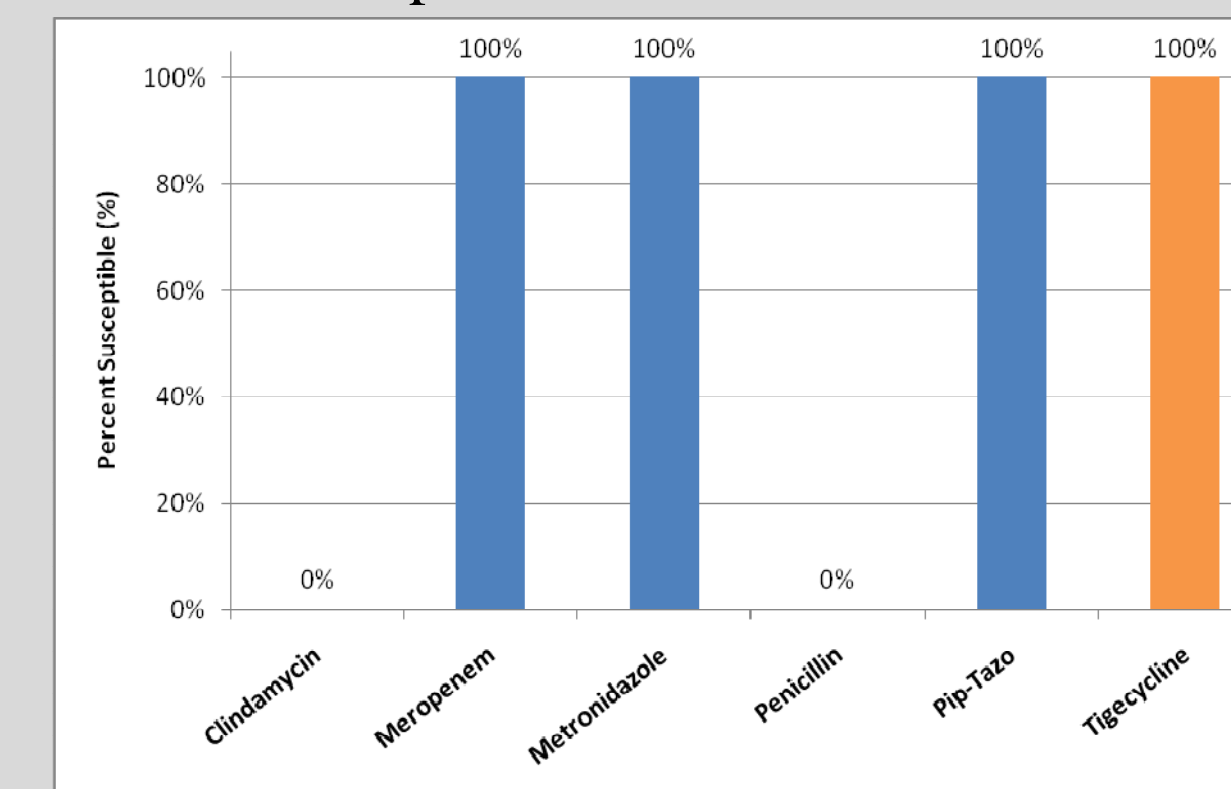


Figure 2. Percent susceptibilities of 128 MDR *Clostridium* isolates.



Conclusions

- ▶ 23.4% of all *Clostridium* isolates from 2007-2008 were MDR.
- ▶ *C. difficile* was the most frequently isolated species comprising 87% of all MDR isolates.
- ▶ Tigecycline exhibited good *in vitro* activity against MDR *Clostridium* spp (MIC₉₀ 0.25 mcg/ml)
- ▶ 100% of MDR *Clostridium* isolates were susceptible to tigecycline, meropenem, piperacillin-tazobactam, and metronidazole at their respective CLSI breakpoints.