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Evaluation of the potential impact of a carbapenem de-escalation program in an academic healthcare system

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Summary The primary objective of this analysis was to evaluate group 2 carbapenem usage and to model the impact that a formalized de-escalation protocol to ertapenem could potentially have on group 2 carbapenem usage in the hope of alleviating the selective pressure on *Acinetobacter* and *Pseudomonas*. This analysis was conducted in three hospitals within the Detroit Medical Center in 2009. Patients were considered candidates for de-escalation of carbapenem therapy when a group 2 carbapenem was utilized to treat Enterobacteriaceae, such as extended spectrum β-lactamase (ESBL)-producing organisms, or if cultures were negative in non-intensive care unit (ICU) patients. In total, 179 patients (28%) and 1074 patient-days (29%) were deemed eligible for de-escalation according to our pre-defined criteria. We concluded that preferential utilization of ertapenem in appropriate patients warranting carbapenem therapy has the potential to significantly decrease group 2 carbapenem usage at our institution.
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Introduction

Resistance to group 2 carbapenems, such as meropenem, imipenem, and doripenem, among *Acinetobacter baumannii* and *Pseudomonas aeruginosa* poses a significant therapeutic

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challenge. Often, the only remaining therapeutic options are tigecycline (for *Acinetobacter* and not *Pseudomonas*) or colistin-based regimens, which are associated with suboptimal outcomes and high rates of toxicity [1—3]. Ertapenem is a group 1 carbapenem that retains good *in vitro* activity against Enterobacteriaceae, including extended spectrum β-lactamase-producers (ESBLs) and ampC hyperproducers [4], but has no appreciable activity against *A. baumannii* or *P. aeruginosa*. Because of this lack of activity against non-lactose-fermenting Gram-negative organisms, there is a potential benefit, in terms of antimicrobial resistance, of using ertapenem in place of group 2 carbapenems to reduce the selective antimicrobial pressure. Recent studies have reported that the susceptibility of *P. aeruginosa* to imipenem remained stable [5—7] and, in some cases, even improved [8] after the introduction of ertapenem into hospital formularies. However, it is important to note that direct causality between ertapenem introduction and the improved susceptibilities in *P. aeruginosa* should not be assumed, as increases or decreases in susceptibility are multifactorial. Despite this caveat, evidence suggests that, at the very least, introduction of ertapenem does not negatively affect imipenem susceptibility in *P. aeruginosa*.

The aims of this study were to analyze the utilization of group 2 carbapenems in a large tertiary healthcare system to identify patients in whom de-escalation from group 2 carbapenem to ertapenem would have been appropriate and to model the potential impact of a formalized carbapenem de-escalation program on carbapenem utilization.

Materials and methods

A retrospective analysis of all carbapenem use at three hospitals within the Detroit Medical Center (DMC) in 2009 was performed. The DMC is a university-affiliated eight-hospital tertiary healthcare system with more than 2200 inpatient beds in metropolitan Detroit. For the purposes of these analyses, only patients at Detroit Receiving Hospital, Harper University Hospital, and Sinai-Grace Hospital were included. These three hospitals have a total of 1180 beds. The pharmacy database was queried to identify all patients at these institutions who received any carbapenem in the 2009 calendar year. The medical records for these patients were then accessed, and a standardized data collection form was utilized to extract the patient demographics, comorbid conditions, intensive care unit (ICU) status, relevant laboratory values, indications for carbapenem therapy, microbiological results, and the doses and durations of therapy.

The charts of the patients who received group 2 carbapenems were analyzed to determine whether de-escalation to ertapenem therapy would have been appropriate. De-escalation was considered appropriate if the patient was receiving therapy for infections due to an ESBL, an ampC-producing organism, or other carbapenem-susceptible Enterobacteriaceae or if the culture was negative and the patient continued to receive therapy; additionally, the patient had to be located on the general medical floor. Patients were deemed ineligible for de-escalation to ertapenem if *P. aeruginosa*, *A. baumannii*, or penicillin-susceptible *Enterococcus* spp. were recovered, if the cultures were negative and they resided in the ICU (as many clinicians desire activity against *P. aeruginosa* in an ICU setting even if cultures are negative) if they received carbapenem therapy for $\leq$72 h following culture, or if the patient had cystic fibrosis, central nervous system infection, febrile neutropenia, osteomyelitis, or infection due to *Nocardia* spp. If patients met the eligibility criteria for de-escalation to ertapenem, the initial 72 h of group 2 carbapenem therapy after culture were considered appropriate, as cultures are often finalized after 72 h.

Analysis was performed to assess the impact that a carbapenem de-escalation program would have on the amounts of group 2 carbapenem and ertapenem utilized during the study period.

Results

Carbapenem utilization

A total of 557 patients received meropenem during the study period, accounting for 3601 patient-days of therapy. Imipenem was used in 42 patients for a total of 223 patient-days, while ertapenem was utilized in 156 patients for 829 patient-days of therapy.

Analysis of group 2 carbapenem usage

Tables 1 and 2 show detailed breakdowns of the group 2 carbapenem usage and cases where de-escalation to ertapenem would have been appropriate (n = 1074 patient-days, 28% of total usage) or inappropriate (n = 2232 patient-days, 58% of total usage). For patients in whom de-escalation therapy would have been appropriate, the first 72 h of the group 2 carbapenem therapy after culture was considered appropriate, and this time accounted for the remaining 528 patient-days (14%) of usage.

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