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Short Communication

Carbapenem use in French hospitals: A nationwide survey at the patient level

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ABSTRACT

The objective of this study was to evaluate the characteristics of carbapenem use in French healthcare settings in order to guide future actions. Healthcare facilities voluntarily participated in a nationwide cross-sectional survey in 2011. Medical data and reasons for carbapenem treatment (CPR) and discontinuation were recorded for all patients treated with carbapenems. A total of 2338 patients were recorded by 207 facilities. The median duration of CPR was 8 days, and 31.4% of patients received CPR for >10 days. An antibiotic consultant was involved in the initial choice of CPR in 36.8% of cases. CPR was chosen on an empirical (EP) basis for 1229 patients (52.6%), mainly because of severe sepsis (48.6%) or a perceived risk of bacterial resistance (33.7%). Among EP patients, de-escalation was more frequent in the case of intervention of an antibiotic consultant (35.1%) than without intervention (22.9%) ($P < 0.01$). Among the 1109 patients receiving CPR initially based on bacteriological results, 607 (54.7%) had ESBL-producing Enterobacteriaceae and 397 (35.8%) had Gram-negative bacilli susceptible to at least one β-lactam other than carbapenems or to fluoroquinolones. Among the latter, de-escalation was performed in 59 cases (14.9%). The intervention of an antibiotic consultant did not favour de-escalation in this group. In conclusion, carbapenems are frequently used for treating suspected or confirmed multidrug-resistant bacteria, and overall CPR duration is long. De-escalation is frequently not implemented despite isolates being susceptible to other drugs. More frequent antibiotic consultant intervention may help to decrease carbapenem use in the case of EP treatment.

1. Introduction

In most part of the world, Gram-negative bacilli (GNB) are the most frequent micro-organisms isolated both from community and nosocomial infections. Among these bacteria, resistance to extended-spectrum cephalosporins (ESCs) has increased over the last decade [1]. In addition, the emergence of CTX-M-type extended-spectrum β-lactamases (ESBLs) has modified the epidemiology of ESC resistance in Enterobacteriaceae since the

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dissemination of ESBL enzymes has occurred in the community as well as in healthcare settings [2].

The consequence of increasing ESC resistance has been a significant rise in the use of antibiotics active against multidrug-resistant (MDR) bacteria, mainly carbapenems. Increased carbapenem use has been followed by an increase in carbapenem-resistant *Pseudomonas aeruginosa* and Enterobacteriaceae [1]. The use of carbapenems in intensive care units has been associated with the emergence of imipenem-resistant GNB in the commensal flora, even after a short treatment duration [3]. In addition, new mechanisms of resistance to carbapenems have emerged in the last decade [4]. Therefore, it is in our interest to limit the use of carbapenems to well-defined indications.

We have previously reported a rather high proportion (7.8%) of carbapenem use among patients treated by antibiotics in French hospitals [5]. Hence, a better understanding of the characteristics of carbapenem prescriptions should help to develop comprehensive recommendations for carbapenem use. Therefore, a cross-sectional survey of carbapenem use at the patient level, including the reasons for carbapenem prescribing, was designed.

2. Methods

2.1. Study design

French healthcare settings collaborating with the French Society of Infectious Diseases (SPILF) (http://www.infectiologie.com) and the French National Observatory for Epidemiology of Bacterial Resistance to Antibiotics (ONERBA) (http://www.onerba.org) were asked to participate on a voluntary basis in an observational study of inpatients receiving a carbapenem-containing regimen during a 3-month period (October–December 2011).

2.2. Data collection

Healthcare settings had to record data for ≥10 consecutive inpatients treated by a carbapenem in all wards of the facility, or all inpatients if <10 cases were eligible during the study period. Data collected included prior history of hospitalisation and antibiotic treatment in the previous 3 months, ward hospitalisation and antibiotic received since admission and before the first carbapenem administration.

Data regarding carbapenem treatment (CPR) included the site of infection, empirical versus targeted treatment, reasons for carbapenem initial choice and cessation as recorded by the prescriber, treatment duration, and re-assessment after 2–3 days and 7–10 days. De-escalation was defined as replacement of a carbapenem by another antibiotic. Microbiological data were the results of culture of clinical samples processed by the local laboratory, including species identification, antimicrobial susceptibility test (AST) results, and testing for production of ESBLs by Enterobacteriaceae following the 2011 recommendations of the French Committee for Antibiogram of the French Society for Microbiology (http://www.sfm-microbiologie.org). In order to assess alternative antibiotics to carbapenems, all GNB from patients with polymicrobial infections were considered as a whole for evaluating antibiotic susceptibilities. Empirical therapy was defined as CPR in patients without documented infection or initiated before the availability of AST results for bacteria isolated from clinical samples.

2.3. Statistical analysis

Data were collected using a standardised website questionnaire. Continuous variables were expressed as median and range and were compared using the Kruskal–Wallis test. Categorical variables were expressed as number and proportions, and the χ^2 test or Fisher's exact test were used as appropriate for comparisons. Statistical analysis was performed using STATA (StataCorp, College Station, TX) and $P < 0.05$ was deemed statistically significant.

3. Results

3.1. Facilities

A total of 251 healthcare facilities (41 teaching hospitals, 175 non-teaching or private hospitals and 35 rehabilitation or long-term care facilities) participated in the study covering 74 (73.3%) of the 101 French departments. They represented 17.7% and 4.8% of acute-care and rehabilitation or long-term care facilities, respectively, and 23% of all French healthcare beds. All but one facility had appointed an antibiotic specialist (AB) consultant. A total of 231 facilities (92.0%) reported controlled access to carbapenems; 195 (77.7%) undertook systematic re-assessment of prescription at 48–72 h and 109 (43.4%) after 7–10 days. Among all facilities, 44 did not record any CPR during the 3-month study period, 102 recorded <10 patients receiving CPR and 105 recorded ≥10 CPR patients.

3.2. Treatment

The 207 facilities included 2338 patients (62.3% male) receiving at least one CPR (Table 1), mainly imipenem ($n = 2051$; 87.7%) and ertapenem ($n = 173$; 7.4%).

The median age of the patients was 67.0 years (0.1–100.0 years) and 24.5% were aged >80 years. A total of 1485 (63.5%) and 1210 (51.8%) patients had a history of prior hospitalisation and antibiotic treatment, respectively; 1637 patients (70.0%) had a history of one of both of these. A total of 1525 patients (65.2%) already received an antibiotic course (86.7% β-lactams) other than a carbapenem since admission and before CPR.

Moreover, 26 patients (1.1%) had CPR on admission, 389 (16.6%) on the day of admission and 975 (41.7%) >10 days after hospital admission. Among the latter, 856 (87.8%) had already been treated by antibiotics since admission (Table 2).

Initial CPR choice was empirical (EP) for 1229 patients (52.6%) and was based on bacteriological results (BR) for the remaining 1109 (47.4%). Among patients from the EP group, 1062 (86.4%) had a prior history of hospitalisation and/or antibiotic use. In the EP group, CPR choice was based on the severity of illness (48.6%) or a perceived risk of resistance to ESCs (33.7%), and 17.7% for other criteria or no reason mentioned. AB consultants were less likely to be consulted for CPR initiation in the EP than in the BR group (32.6% vs. 41.5%; $P < 0.001$).

The median duration of CPR was 8 days (1–188 days) and it was longer for the BR group (9 days) than for the EP group (6 days) ($P < 0.001$). Patients receiving CPR for >10 days ($n = 735$; 31.4%) were mainly treated for urinary tract infections (26.1%), pulmonary infections (22.3%) and intra-abdominal infections (11.3%). Among the 141 patients (19.2%) with other infections, 53 (7.2%) had bone and joints infections and 5 (0.7%) had endocarditis. There was no statistical difference in the CPR duration for patients treated for the three main infections with or without AB consultants.

For 1643 patients (70.3%), the carbapenem was combined with at least one antibiotic, and this proportion was higher in the EP group (74.9%) than in the BR group (65.1%) ($P < 0.001$). However, only 59.8% of the patients received an antibiotic combination active against GNB. The carbapenem was associated with an aminoglycoside in 932 cases (56.7%) and with a fluoroquinolone in 431 cases (26.2%). The median treatment duration with the combined antibiotics was longer in the BR group than in the EP group, either for aminoglycosides (3 days vs. 2 days; $P < 0.001$) or for fluoroquinolones (11 days vs. 7 days; $P < 0.001$).

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