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Original article

Cessation of screening for intestinal carriage of extended-spectrum β-lactamase-producing *Enterobacteriaceae* in a low-endemicity intensive care unit with universal contact precautions

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ABSTRACT

Objectives: The usefulness of screening for carriage of extended-spectrum β-lactamase-producing *Enterobacteriaceae* (ESBL-E) with active surveillance cultures (ASC) remains equivocal in low-endemicity intensive care units (ICUs). Our primary objective was to appraise the impact of ceasing ASC on the incidence of ICU-acquired ESBL-E infections in an ICU with universal contact precautions (CP). Patient outcomes and carbapenem consumption were also investigated.

Methods: A single-ICU, retrospective, uncontrolled before-and-after study including all patients admitted for ≥3 days during two consecutive 1-year periods with and without ASC.

Results: A total of 524 and 545 patients were included during the ASC and the no-ASC periods, respectively. Twenty-eight patients (5.3%) from the ASC period were ESBL-E carriers. An ICU-acquired ESBL-E infection (median duration of risk exposure, 4 (range 2–9) days for both periods) occurred in 1.1% and 1.5% of patients admitted during the ASC and the no-ASC periods ($p = 0.64$), with no inter-period variation in incidence after adjustment on competing risks of death and ICU discharge (standardized hazard ratio (SHR) 2.32, 95% CI 0.80–6.73, $p = 0.12$). An admission during the no-ASC period exerted no independent impact on the hazards of ESBL-E infections (adjusted OR 1.16, 95% CI 0.38–3.50, $p = 0.79$), in-ICU death (SHR 1.22, 95% CI 0.93–1.59, $p = 0.15$) and extended length of stay (SHR for discharge 0.89, 95% CI 0.79–1.01, $p = 0.08$). Carbapenem exposure in patients without ESBL-E infection decreased between the ASC and no-ASC periods (75 versus 61 carbapenem-days per 1000 patient-days, $p = 0.01$).

Conclusions: In a low-endemicity ICU with universal CP, the withdrawal of routine screening for ESBL-E carriage had no significant effect on the incidence of ICU-acquired ESBL-E infections and patient outcomes. Carbapenem consumption decreased in patients without ESBL-E infection. **W. Jalalzaï, Clin Microbiol Infect 2017;▪:1**

Introduction

The dissemination of extended-spectrum β-lactamase-producing *Enterobacteriaceae* (ESBL-E) constitutes a growing challenge for the management of patients admitted to the intensive care unit (ICU) [1]. Compared with those involving broad-spectrum cephalosporin-susceptible *Enterobacteriaceae*, ICU-acquired infections due to ESBL-E heighten the hazard of dying, extend the ICU stay, and induce a substantial rise in carbapenem consumption that may hasten the diffusion of carbapenem-resistant Gram-negative pathogens in the critical care environment [2–5]. The prevention of ESBL-E cross-transmission among ICU patients is therefore a pivotal issue.

The gut microbiota acts as the main reservoir of pathogenic ESBL-E strains in critically ill patients [6–8]. Hence, academic infection prevention guidelines advocate the universal use of active surveillance cultures (ASC) for the detection of intestinal carriage of ESBL-E in ICUs facing endemicity or outbreaks, with the application of contact precautions (CP) in identified carriers [9–11]. In addition

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to hand hygiene and other standard precautions, CP bundles usually include the utilization of a single-bed room and patient-dedicated equipment, the wearing of single-use gloves and gowns for healthcare workers during contacts with colonized patients or contaminated environment, and the signalization of carriage to reinforce compliance [9–11]. Nonetheless, it remains unclear whether such a screening strategy may help to contain the spread of ESBL-E in relatively low-prevalence settings with otherwise optimized prevention measures [12–16]. Besides, the volume of rectal samples inherent to a protocol of routine ASC generates a massive workload for laboratory staff and a high financial burden for the hospital system [17].

In our ICU, standard infection prevention measures meet the definition of CP for every admitted patient. The prevalence of ESBL-E carriage has remained consistently low over recent years (range 5%–7%), with no detectable episode of outbreak [18]. On April 2014, the decision to withdraw the policy of systematic screening for ESBL-E carriage was reached following conciliation with the institutional infection control unit. In this study, we sought to appraise the impact of ASC cessation on three end points; namely, the incidence of ICU-acquired ESBL-E infections, overall carbapenem consumption and patient outcomes.

Patients and methods

Study setting: ICU characteristics

This single-centre study was conducted in the 18-bed medical–surgical ICU of a 1100-bed teaching hospital in France. The ICU comprises only single-bed rooms with a 1 : 2.5 nurse-to-patient ratio and patient-dedicated equipment for care, monitoring and mobilization. In addition to hand hygiene with alcohol-based hand-rub-based hand hygiene (at room entrance and exit, and between each distinct procedure of care), the standard policy for infection prevention entails: (a) the use of single-use gloves and gowns in case of close contact with patients and potential exposure to body fluids during nursing, physiotherapy and other care not requiring full-barrier precautions, and (b) a twice-daily cleaning of all inert surfaces from the patient's environment using a quaternary ammonium-based disinfectant. These measures were equally applied during both inclusion periods (see below).

Patients admitted until April 2014 were routinely screened for ESBL-E carriage by rectal swabbing at admission then weekly afterwards. Imported carriage was defined as a positive rectal swab within the 48 hours following admission, whereas acquired carriage was defined as a positive surveillance swab in patients with a negative admission sample. Details on swab processing and ESBL-E detection are available in the Supplementary material. ESBL-E carriage was signalled, but isolation measures remained identical whatever the colonization status.

In this ICU, the empirical regimen for a first episode of ICU-acquired infection usually combines high-dose piperacillin-tazobactam (16 g/2 g daily by extended or continuous infusion in patients with normal renal function) and amikacin (25 mg/kg), plus vancomycin or linezolid when β-lactam-resistant Gram-positive pathogens are suspected. The empirical use of carbapenems is restricted to patients with previous exposure to an anti-pseudomonal β-lactam during the hospital stay or a previous sample positive with Gram-negative pathogens exhibiting resistance to all broad-spectrum β-lactams except carbapenems.

Study design and patient population

This was a retrospective, uncontrolled before-and-after study. We included all patients with a first ICU stay of more than two calendar days during two 1-year periods: a first period with universal ASC for the detection of ESBL-E carriage (from 1 April 2013 to 31 March 2014) then a second period starting 6 months after ASC cessation (from 1 September 2014 to 31 August 2015). Eligible patients were screened using admission registries. The three aforementioned study end points were addressed by comparing patients admitted during the ASC period and the no-ASC period, with the incidence of ICU-acquired ESBL-E infections as the primary outcome. Definitions and procedures for data collection are detailed in the Supplementary material. The institutional review board waived the requirement for informed consent (IRB report no. 2016-10). This study is reported according to the STROBE guidelines [19].

Statistical analysis

Data are expressed as median (interquartile range) for continuous variables and number (%) for categorical variables, unless indicated. Antimicrobial consumption was measured for both periods as the total number of treatment days with a given class/total number of patient-days in the ICU × 1000. Patients were compared using the Student's *t*-test or the Mann–Whitney *U*-test for continuous variables and the Fisher exact test or the chi-squared test for categorical variables, as appropriate.

To investigate whether being admitted during the no-ASC period was associated with an increased hazard of ICU-acquired ESBL-E infection, we first performed univariate analyses to search for a significant association between each variable and the occurrence of these infections. Variables yielding p values <0.20 were then entered into a multiple logistic regression model (stepwise procedure) for the measurement of odds ratios (OR) and 95% confidence interval (CI) with the occurrence of ICU-acquired ESBL-E infection as the primary outcome. An inclusion during the no-ASC period was forced into this multivariate model. Next, we compared the cumulative incidence of ICU-acquired ESBL-E infections during the two periods using a Fine and Gray model with death or ICU discharge handled as competing events [20]. Lastly, we assessed whether an inclusion during the no-ASC period was independently associated with an increase in the cumulative incidence of in-ICU death after adjustment on the Simplified Acute Physiology Score II (SAPS II) value at ICU admission and considering ICU discharge as a competing event. All tests were two-sided, and p values <0.05 were considered significant. Analyses were carried out using the R 2.15.1 software (http://www.r-project.org).

Results

Study population

A total of 1069 patients were entered in the study cohort, including 524 patients during the ASC period and 545 patients during the no-ASC period (see Supplementary material, Fig. S1). Patient characteristics are given in Table 1 and in the Supplementary material (Table S1) and did not show any prominent differences between the two groups. Most patients (84.1%) were admitted directly from the Emergency Department.

ESBL-E carriage during the ASC period

A total of 863 rectal swabs (estimated crude cost, € 13 980) were collected during the ASC period (admission swabs, $n = 524$; weekly surveillance swabs, $n = 339$). Twenty-eight patients (5.3%) were identified as ESBL-E carriers, including 17 (3.2%) with imported carriage and 11 (2.1%) with ICU-acquired carriage (acquisition rate, 2.4 events per 1000 patient-days). *Escherichia coli* ($n = 16$) and

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