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Changing third-generation cephalosporin policy reduces methicillin-resistant *Staphylococcus aureus* and extended-spectrum beta-lactamase-producing *Enterobacteriaceae* nosocomial infections rates

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Background: Healthcare-associated infections (HAI) with multidrug-resistant bacteria (MRB) are a major public health threat. Alcohol-based hand hygiene and antibiotic stewardship are the cornerstone to control antibiotic resistance. In particular, promoting use of antibiotics with low biliary elimination could limit the selection of MRB.

Material/methods: An intervention was implemented after January 2014 in a 350-bed general hospital in Lyon (France) to change the antibiotic prescription policy by promoting cefotaxime (CTX) use instead of ceftriaxone (CRO). Here, we retrospectively assess the impact of this intervention on monthly MRB HAI incidence, using 6-year longitudinal data collected from January 2011 to December 2016 from the biological, pharmaceutical, hospital hygiene and medical information departments. Before/after intervention comparisons are performed. Monthly incidences of HAI with extended-spectrum β -lactamase-producing (ESBL) Enterobacteriaceae or methicillin-resistant *Staphylococcus aureus* (MRSA) with or without bloodstream microbial identification, *Clostridium difficile* HAI and *Candida* fungal bloodstream HAI are analyzed using generalized estimating equations with a multivariate Poisson regression model.

Results: Following the intervention, CRO consumption significantly decreased (45.6 ± 5.0 vs. 15.3 ± 10.1 defined daily doses/1000 patients-occupied bed-days (DDDs/1000 PBDs); $p < 0.001$) while CTX consumption increased (8.7 ± 6.2 vs 45.6 ± 5.0 DDDs/1000 PBDs; $p < 0.001$). Global antibiotic consumption remained stable.

In the intensive-care unit, ESBL Enterobacteriaceae HAI significantly decreased after the intervention (5.17 ± 3.39 vs 3.14 ± 4.27 cases/1000 PBDs; $p = 0.004$) while ESBL Enterobacteriaceae rectal carriage at admission doubled (0.27 ± 0.22 vs 0.63 ± 0.31 cases/1000 PBDs; $p < 0.001$). No significant difference was found when comparing MRB HAI incidence before and after the intervention throughout the hospital.

With multivariate analyses however, the intervention was associated with a significant reduction in MRSA HAI in the entire hospital ($p = 0.005$), as well as with a significant decrease in ESBL Enterobacteriaceae HAI ($p = 0.001$) and in MRSA HAI ($p = 0.01$) in the intensive-care unit.

Other significant factors associated with the incidence of MRB HAI throughout the hospital were: number of dialysis, number of post-emergency admissions, and alcohol-based hand rub consumption for ESBL Enterobacteriaceae HAI; number of dialysis, nasal MRSA carriage at admission, amoxicillin-clavulanate, carbapenem and macrolide consumption for MRSA HAI; and amoxicillin-clavulanate consumption and number of patients with cancer for *Candida* fungal bloodstream HAI.

Conclusions: Even in a hospital with low incidence of MRB HAI, a switch from ceftriaxone to cefotaxime may still have a significant impact on the incidence of MRSA and ESBL Enterobacteriaceae infections, especially in the intensive-care unit. This underlines the importance of antibiotic stewardship to control MRB spread.