

Changing Third-Generation Cephalosporins policy reduces Methicillin-Resistant *Staphylococcus aureus* and Extended-Spectrum β -Lactamase-producing Enterobacteriaceae nosocomial infections

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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.

Methods: An intervention was implemented since 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. And linear trend terms were used to assess temporal changes with interrupted time series analysis.

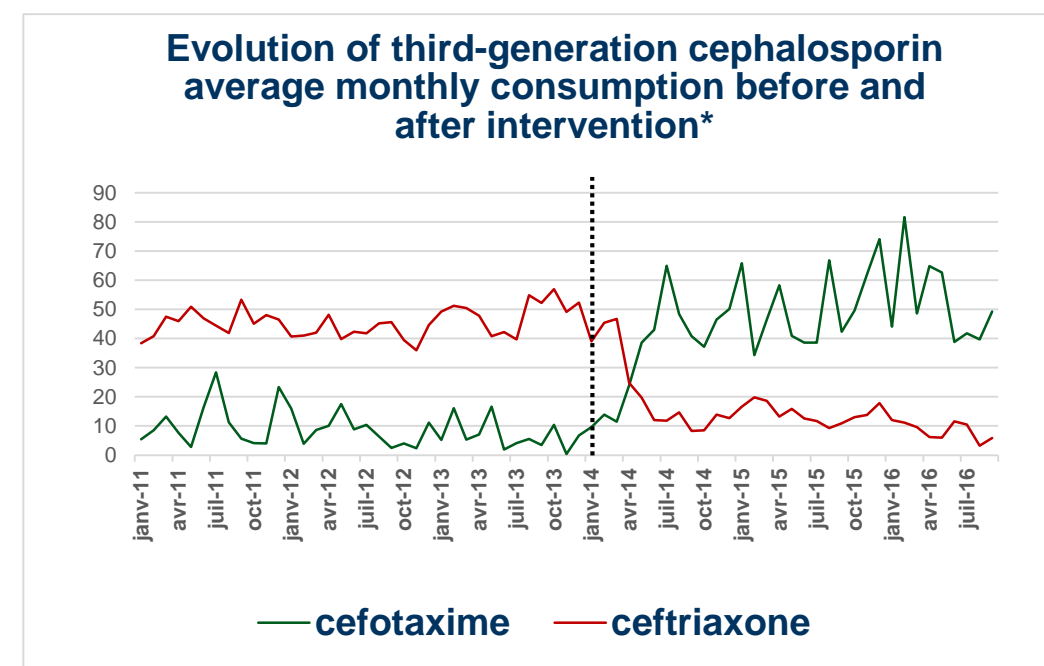
References

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Results

Hospital consumption	Before intervention	After intervention	p-value
Alcohol-based solution	88 156 ml	57 147 ml	0.005
Antibiotics total*	612.7 ± 65.8	618 ± 79.4	0.68
Penicillin A*	121 ± 38.5	122 ± 31.3	0.93
Penicillin A-clavulanate*	143.4 ± 29.7	136.7 ± 27.8	0.52
Piperacillin-tazobactam*	15.1 ± 3.8	19 ± 6.6	0.006
Carbapenems*	14.9 ± 8.8	9.9 ± 5.3	0.007
Fluoroquinolones*	57.9 ± 14.8	47.2 ± 12.2	0.002
Ciprofloxacin*	17.5 ± 7.9	31 ± 36.1	0.58
Gentamicin*	12.7 ± 8.5	34.3 ± 41.3	0.05
Amikacin*	9.6 ± 8.9	29.7 ± 9.6	0.03
Macrolides*	19.4 ± 6.8	15.6 ± 6.9	0.02

Following the intervention, CRO consumption significantly decreased (45.6 ± 5.0 vs. 15.3 ± 9.7 defined daily doses/1000 patients-occupied bed-days (DDD/1000 PBDs); $p < 0.001$) while CTX consumption increased (8.7 ± 6.2 vs 46.8 ± 16.3 DDD/1000 PBDs; $p < 0.001$). Global antibiotic consumption remained stable.



No significant difference was found when comparing MRB HAI incidence before and after the intervention over the entire hospital but **ESBL-producing Enterobacteriaceae HAI significantly decreased only in intensive care unit** (5.2 ± 3.4 vs 2.9 ± 4 cases/1000 PBDs $p = 0.01$) while **ESBL Enterobacteriaceae rectal carriage at admission doubled** (6.3 ± 5.3 vs 13.3 ± 7.5 cases/1000 PBDs ; $p < 0.001$).

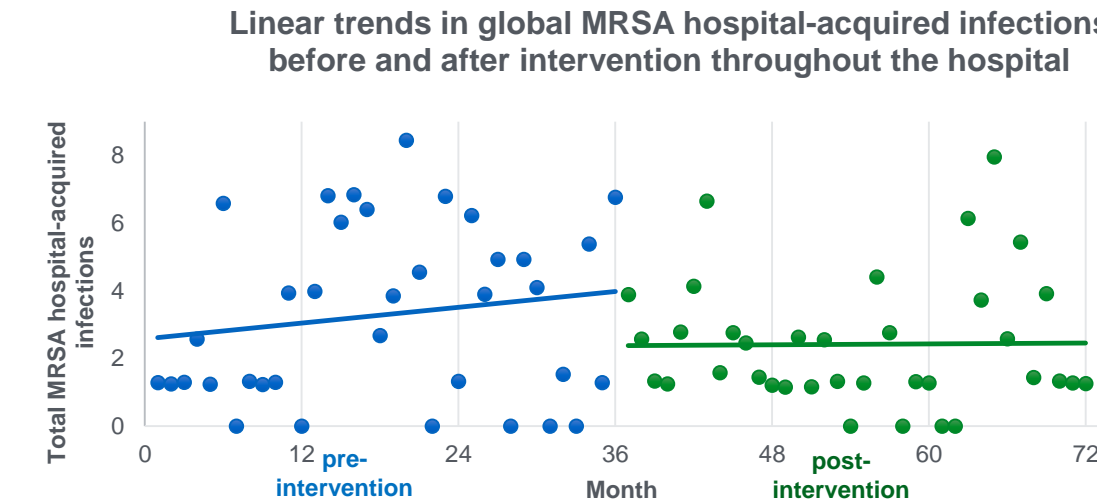
In multivariate analysis however, the intervention was associated with a **significant reduction in MRSA HAI throughout the hospital** ($p = 0.005$), as well as with a **significant decrease in ESBL-producing Enterobacteriaceae resistant** ($p < 0.001$) **Enterobacteriaceae HAI in the intensive-care unit**.

Other factors associated with the incidence of for ESBL Enterobacteriaceae HAI throughout the hospital were: number of chemotherapy, consumption of carbapenems, and alcohol-based hand rub consumption.

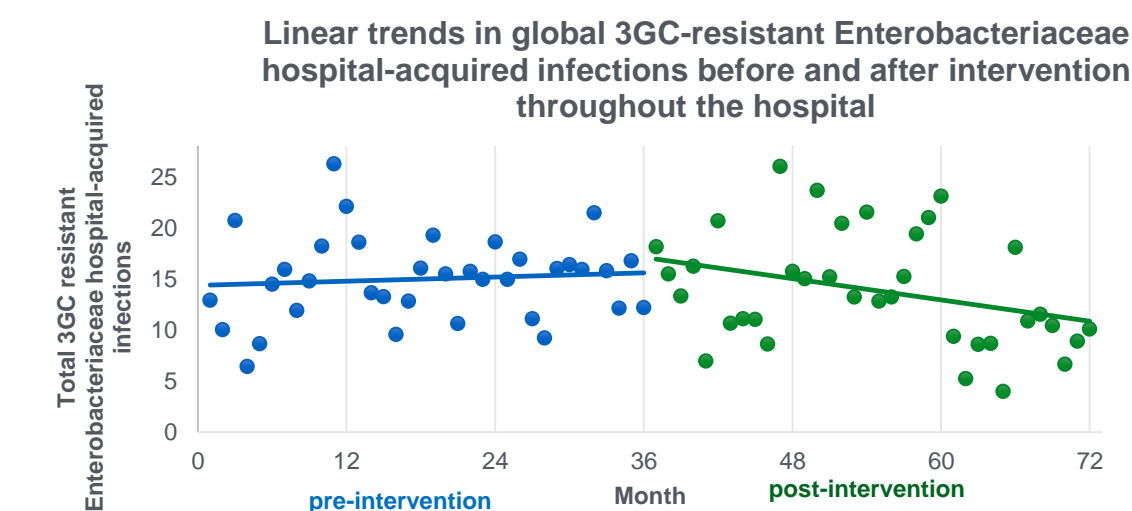
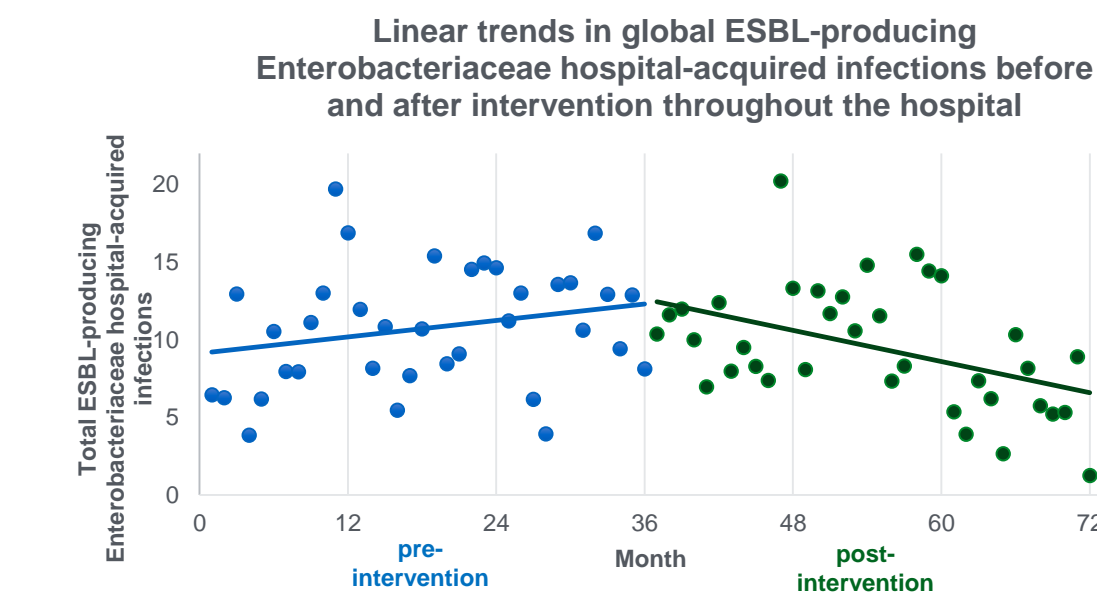
ICU independent factors associated with ESBL-producing coliforms HAI in multivariate analysis	Coefficient	p-value (Poisson regression)	CI 95%
Length of urinary catheter	0.3	0.03	0.03 ; 0.63
Central venous catheter insertion	0.07	<0.001	0.02 ; 0.12
SAPS II	- 0.09	0.007	- 0.1 ; - 0.02
Initial rectal ESBL carriage	0.2	<0.001	0.1 ; 0.3
Intervention	- 1.6	<0.001	- 2.4 ; - 0.9

ICU invasive procedures	before intervention	after intervention	p-value
Number of central venous catheter insertion	20.4	23.3	0.04
Number of oro-tracheal intubation	13.8	15.6	0.12
Invasive mechanical ventilation	154.9 days/month	171.2 days/month	0.21
Number of dialysis	22.5	28.5	0.07
Length of exposition to urinary catheter	9.9 days	11.2 days	<0.001

*defined daily dose / 1000 patients-bed-days



Trends in our MRSA HAI results throughout the hospital could be related to a current regional and national significant decreases in MRSA HAI incidence. And our multivariate analysis could not integrate it in our monocentric study.



Conclusion

Even in a hospital with low incidence of multidrug-resistant bacteria hospital-acquired infections, **a switch from ceftriaxone to cefotaxime may still have a significant impact on the incidence of ESBL-producing Enterobacteriaceae hospital-acquired infections, especially in the intensive-care unit**. This underlines the importance of antibiotic stewardship to control multidrug-resistant bacteria spread.