

Trend of antibiotic resistances compared to antibiotic consumption at a referral university hospital during a 7-year period (2008-2014)

Monticelli Jacopo¹, Simonetti Omar¹, Mascarello Marta¹, Buseti Marina², Knezevich Anna², Torelli Lucio³, Schincariol Paolo⁴, Luzzati Roberto¹.

Universitary Hospital of Trieste, Italy. 1: Infectious Diseases Unit; 2: Microbiology and Virology Department; 3: Life Sciences Department; 4: Hospital Pharmacy.

Background: The misuse of antibiotics selects resistant strains of the majority of health-care associated (HCA) bacteria. The control of antibiotic consumption and resistance remains crucial in the hospital setting.

Objectives: The aim of this study was to investigate the potential correlation between antibiotic consumption and antimicrobial resistance of bacteria more commonly associated with HCA bloodstream infections.

Methods: We evaluated retrospectively susceptibility data regarding all consecutive bloodstream isolates of *S. aureus*, *E. faecalis*, *E. faecium*, *E. coli*, *Klebsiella spp*, *Proteus spp*, *P. aeruginosa*, *A. baumannii* during the period 2008-2014 at the university hospital of Trieste, Italy. Likewise, consumption of main antibiotics for systemic usage were registered along the same time period. Percentage of antibiotic resistance and Defined Daily Dose (DDD)/100 patient-day were chosen as standard units for evaluating antibiotic resistance and consumption, respectively. Secular trends were analyzed independently and correlations between antibiotic consumption and percentages of resistance was investigated through a Pearson's correlation.

Results: Rates of oxacillin-, levofloxacin- and gentamicin-resistant *S. aureus* isolates significantly decreased from 2008 to 2014: 49% to 26% (p-value=0.02), 51% to 23% (p-value=0.03), 42% to 23% (p-value=0.06), respectively. Rates of ESBL-positive *Klebsiella spp*. significantly decreased as well: 22% to 0% (p-value=0.03). By contrast, significant increase of resistance rates of *E. coli* to amikacin was found: 3% to 11% (p-value=0.01). In addition, rates of XDR-*A. baumannii* isolates significantly increased (0% to 96%, p-value=0.01) while vancomycin-resistant *E. faecium* (VRE) increased from 0% in 2013 to 10% in 2014 (not linear). Regarding antibiotic consumption a significant increasing trend was detected from 2008 to 2014 for aminopenicillins (24 to 33 DDD/100 patient-day, p-value=0.003), piperacillin/tazobactam (4.1 to 5.7 DDD/100 patient-day, p-value=0.02) and carbapenems (2.6 to 5 DDD/100 patient-day, p-value=0.01) while a reduction was found for gentamicin (1.2 to 0.9 DDD/100 patient-day, p-value=0.02) and fluoroquinolones (16.5 to 15.4 DDD/100 patient-day, p-value=0.06).

A positive correlation was found between *S. aureus*, *E. coli* and *Klebsiella spp* gentamicin-resistance versus gentamicin consumption (p-values 0.05, 0.03, 0.02, respectively); between ESBL-positive *Klebsiella spp* and cefotaxime consumption (p-value=0.02); between XDR *A. baumannii* and cefepime consumption (p-value=0.01). Interestingly, a negative correlation was discovered between oxacillin-resistant *S. aureus* (MRSA) and aminopenicillin consumption (p-value=0.001) (Figure).

Conclusions: Despite a global increased consumption of antibiotics along the 7-year period, this observational study shows decreased rates of MRSA and ESBL-positive *Klebsiella spp* isolates causing bloodstream infections. On the contrary, alarming increased rates of XDR-*A. baumannii* and VRE isolates were reported at the same time. The increasing consumption of aminopenicillins, especially amoxicillin/clavulanate, and the correlated decreasing rates of MRSA isolates is encouraging and needs further investigation.

