O001

2-hour Oral Session

Advancing hospital antibiotic stewardship

Selection of antibiotic-resistant bacteria is a predictable, severe, adverse drug event of the most used antibiotics in hospitalized patients

A. Gorska[1], G. Marasca[2], W. Schröder[2], E. Tacconelli[2]

[1]*Bioinformatics- Tübingen University, Tübingen, Germany*

[2]*Infectious Diseases- University Hospital Tübingen, Tübingen, Germany*

Background: According to WHO and FDA, an adverse drug event (ADE) is an injury caused by taking a drug which is noxious and unintended, and which occurs at doses normally used for therapy. Recently, an increasing number of reports showed a significant association between antibiotics usage and development of resistance. Nevertheless, RCTs for new antibiotics approval are not designed to evaluate selection for resistance among the side effects.
Objectives: The primary study end point was the evaluation of the incidence of selection of antibiotic-resistant strains in hospitalized patients after starting antibiotics. Secondary end point was the severity of the event according to the FDA severity score for ADE.
Methods: Two-year multicenter prospective European cohort study. Target microorganisms were: methicillin-resistant *Staphylococcus aureus* (MRSA), ESBL-producers *Enterobacteriaceae*, and carbapenemase-resistant *Pseudomonas* and *Acinetobacter* (here indicated as MDR-GN). The incidence of the ADE was defined according to the FDA scale (very common ≥10%; common > 1% < 10%; uncommon > 0.1% - < 1%; rare < 0.1%) and checked through periodic nasal and rectal screening (baseline, after 3, 7, 14 and 30 days of therapy). Severity of the ADE included: death, length of hospitalization (LOS), disability, and requirement of intervention to prevent permanent impairment or damage. The incidence of the ADE was analysed by single drug, class, and combinations (carbapenems / other beta-lactams; aminoglycosides / beta-lactams; and carbapenems / quinolones). Patients not undertaking antibiotics were used for the analysis of confounders.
Results: Overall 10,197 patients were included in the study providing 58,804 samples. At baseline 8,933 patients were not colonised by MRSA or MDR-GN. Among those, 4,160 started antibiotics for a total of 46,190 observed days of therapy. Monotherapy included: 17,420 days of cephalosporins, 8,030 of quinolones, 3,502 of carbapenems, 2,865 of glycopeptides, 1,803 of aminoglycosides, and 1,387 of macrolides. According to the FDA definition, selection of MRSA was a common event for macrolides usage (7.2% of patients), aminoglycosides (6.5%), carbapenems / quinolones (6.9%), carbapenems (5.4%), and cephalosporins (5.3%). Selection of MDR-GN was a very common event during therapy with cephalosporins (37.3% of patients), anti-anaerobes (34%), carbapenems / other beta-lactams (31%), and quinolones (20.6%). Severity of the event was associated to significantly prolonged LOS (days, ±SD) among patients under antibiotics (13±4 vs 19±12 for MRSA and 12±11 vs 16±12; p<.01 for MDR-GN).
Conclusions: This study is the largest investigation ever conducted to assess association between antibiotic treatment and selection of resistant strains applying the FDA definition for ADE. Current evidence suggests that selection of antibiotic-resistant bacteria is a very common, predictable, severe type A adverse effect of the most common used antibiotics in hospitalised patients. Evaluation of new antibiotics as well as antimicrobial stewardship programme should urgently include this parameter into their implementation process.