

O231

1-hour Oral Session

Modelling and metaanalyses of antimicrobial stewardship efficacy

Clinical effectiveness of antimicrobial stewardship in reducing antibiotic resistance rate: a meta-analysis

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Background: Antibiotic stewardship programmes (ASPs) have proven to reduce antibiotic usage and hospital costs. However, clinical impact of ASPs programme on antibiotic resistant infections and *Clostridium difficile* rates are not clearly defined. Our objective was to perform a meta-analysis of published studies to assess the effectiveness of ASPs on resistance and *C. difficile* infections rates in hospitalized patients.

Material/methods: Searches of PubMed and Cochrane review databases were conducted to find all published studies on ASPs in hospitalized patients till December 2014. Interventions in long term facilities were excluded. Two investigators independently assessed study eligibility and extracted data. The primary outcome was the incidence rate (IR) of antibiotic resistant infections and/or colonisation. IR ratio (IRR) was measured as rate of infection and/or colonisation with antibiotic resistant bacteria per 1.000 patient days. IRR were pooled using random effects models. Random effects estimates of the IRR were modeled on the overall study population as well as stratified by bacteria, antibiotic resistance type, infection or colonisation, study setting, geographical location, and type of intervention (monointervention vs bundled). Heterogeneity was evaluated using I^2 statistic.

Results: Of the 737 unique studies that were reviewed in detail, 21 studies (13 prospective and 8 retrospective) met the study criteria. Overall, 54 outcomes, 18,346 patients and 4,184.073 patient-days were analysed. The implementation of ASPs reduced the antimicrobial resistance rate and *C. difficile* in hospitalized patients by 34% (IRR, 0.66; 95% confidence interval [CI], 0.47-0.93; $p=0.02$) and 62% (IRR, 0.38; 95% CI, 0.23-0.65; $p<0.001$), respectively. A substantial heterogeneity was detected among studies reporting on antimicrobial resistance rate ($I^2=97\%$) while the 4 studies on *C. difficile* showed no heterogeneity. To reduce heterogeneity subgroups stratification and metaregression were applied. Effectiveness of ASPs was more relevant in reducing antimicrobial resistance among gram-positive (43%) than gram-negative bacteria (28%). Stratifying by microorganisms, ASPs were most effective in reducing MRSA (49%, IRR, 0.51; 95% CI, 0.33-0.80) and carbapenem-resistant gram-negative bacteria (48%, IRR, 0.52; 95% CI, 0.32-0.84). No effect was reported on VRE rates while a not significant reduction-trend was observed for ESBL+Enterobacteriaceae (72%) and cephalosporin-resistant gram-negative bacteria (10%). Adjusting for type of resistance, the effect was higher in carbapenem- than in cephalosporin-resistance (39% vs 10%). Effect was slightly higher in reducing colonization as compared to infections (37% vs 26%) and among medical as compared to ICU patients (42% vs 31%). Geographical location and type of intervention (mono-intervention vs bundled) did not impact effectiveness.

Conclusions: This meta-analysis shows clearly that ASPs is highly effective in reducing colonisation and infection rate due to *C. difficile*, MRSA and carbapenem-resistant gram-negative among patients hospitalised in medical wards. These results provide essential information for planning new ASPs in hospitals and underline the importance of microorganism and patient-target ASPs interventions.