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Carbapenemase challenges: mechanisms of action, transmission and control

Antimicrobial stewardship and universal screening are essential components of a stepwise approach to contain the spread of carbapenemase producing *Klebsiella pneumoniae* (CPKP)

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Background: Evidence to contain the spread of carbapenemase producing *Klebsiella pneumoniae* (CPKP) is currently very poor and bundles of infection control intervention are not clearly defined

Material/methods: A quasi-experimental, before and after, interrupted time series analysis from 2012 to 2014 in an 800-beds university hospital with endemic prevalence of CPKP. Three bundles were compared: 1. Room isolation of positive clinical samples in all hospital (2009-2011); 2. Search and destroy strategy in high risk wards and audit of hand hygiene compliance (2012-2013); 3. Universal screening in high risk wards and antibiotic stewardship (ATBS) focused on restriction of carbapenem usage (2014). Incidence of colonisations and infections due to CPKP, hand hygiene compliance by direct observations and by alcohol-based hand rub (AHR) consumption, number of screening for CPKP carriage submitted, and antibiotic consumption defined by daily dose (DDD) were used for the analysis.

Results: During the study period we isolated a total of 1033 CPKP cultures from different specimens: rectal swab 650 (63.3%), urine 216 (21.8%), respiratory tract 58 (5.7%), bloodstream 30 (2.9%). The most common Carbapenemases observed in our study was the Class A carbapenemases (68.8%), Class B beta-lactamases was detected in 12.2%, while Class D beta-lactamases, usually OXA-48, only in 2.2%. 5360 screening were sent in period 2 and 11579 in period 3. The stepwise introduction of bundles showed a progressive decrease of the IR for colonisation and infection all over the hospital. After the introduction of the third bundle CRKP incidence rate showed a decrease of 42% for colonisation and of 79% for BSI ($p < 0.001$). IRR for bundle 2 and for bundle 3 vs bundle 1 were 0.77 (95% CI 0.61–0.98, $p = 0.034$) and 0.58 (0.45–0.75, $p < 0.001$), respectively. The IR for BSI per 1000 bed-days decreased from 0.04 (95% CI 0.02–0.08) to 0.01 (0.001–0.03). IRR for bundle 2 and for

bundle 3 vs bundle 1 were 0.73 (95% CI 0.28– 1.92, p=0.525) and 0.21 (0.04–0.98, p=0.045), respectively. The application of the bundle was more efficient in reducing infections due to CRKP than due to Acinetobacter carbapenem resistant (79% vs 60%).

The AHR consumption trend, expressed as L/1000 bed-days increased from 0.95 L/bed-days to 20 L/bed-days. The total AOU Policlinico Carbapenem DDDs was 4.9 in January 2012, 7.0 on 2013, and 3.5 on December 2014. No significant increase was observed for other antibiotic classes. The bundles did not affect the rate of MRSA BSI infections.

Conclusions: Reduction of incidence rate of CRKP colonisation and infections is possible in high endemic setting after the introduction a multifaceted intervention. Universal screening of high risk wards in association with ATBS seems to play a pivotal role.