O191
Oral Session
Healthcare - associated infections - from analysis to interventions

DESIGN AND ANALYSIS FEASIBILITY OF AN INTERNATIONAL COHORT STUDY OF BACTERAEMIA DUE TO ESBL AND CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE: THE INCREMENT PROJECT.OR619

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OBJECTIVES. To show the ability of an international retrospective cohort study aimed at assessing the efficacy of different antibiotic regimens for bloodstream infections (BSI) due to ESBL-producing *Enterobacteriaceae* (EPE) and carbapenemase-producing *Enterobacteriaceae* (CPR). We used an advanced observational design to determine if pre-designed hypotheses regarding the efficacy of therapy are achievable with the available data.

METHODS. A multinational, retrospective cohort study including sets of consecutive patients with mono-microbial bacteraemia due to EPE or CPE occurring between January 2004 and December 2012 was designed. Thirty-two hospitals from 12 countries are participating. The project was approved by the coordinating centre Institutional Review Board. The main outcome variable was cure rate at day 14; secondary outcome variables included clinical improvement at 72 hours and mortality at 30 days. Independent variables included demographics, severity of underlying and acute conditions, type of acquisition, BSI source, severity of sepsis at presentation, microorganism, type of beta-lactamase, MIC, empirical and targeted therapy. Data are anonymised and included in an online database with restricted access (www.incrementproject.org). The hypotheses to test (basically related to comparison of specific therapeutic empirical and definitive regimens) and the statistical analysis plan, including multivariate analysis using propensity scores, are pre-defined and registered in ClinicalTrials.gov.

RESULTS. Our study includes 835 and 376 episodes of EPE and CRE, respectively. Microorganisms were (EPE and CRE): *E. coli,* 68.2% and 3.9%; *Klebsiella* spp., 24.5% and 80.3%; and other enterobacteria in 7.4% and 15.8%. Urinary and non-urinary tract source accounted for 41.5% and 58.5% of EPE and 12.5% and 87.5% of CRE episodes, respectively. The most frequent ESBLs are CTX-M-14 (21.1%) and CTX-M-15 (18.9%), and the most frequent carbapenemases groups are KPC (76%), VIM (12.7%) and OXA (10.4%). The numbers of included cases per strata according to pre-defined hypotheses are shown in the Table. Outcome data are still crude and comparisons were not directly performed.

CONCLUSIONS. This multinational consortium has gathered the largest sample to date of BSI episodes caused by EPE and CRE. Most of pre-defined hypothesis can be successfully tested with the available data.

Comparison groups	No. of episodes	14-day cure rate	30-day mortality
EPE (Definitive therapy)			
Carbapenems	425	49.2 %	10.6 %
BLBLI	97	58.8 %	8.3 %
Fluoroquinolones	31	67.8 %	3.2 %
Cephalosporins (SI)	12	41.7 %	16.7 %
AG in combination	98	35.7 %	16.3 %
CPE (Definitive therapy)			
Combination therapy	121	22.3 %	38 %
Monotherapy	134	38.1 %	26.9 %
Carbapenem (SII)	50	32 %	26 %
Carbapenem (RI)	54	37 %	44.4 %
Colistin (LD)	69	14.5 %	56.5 %
Colistin (HD)	23	30.4 %	39.1 %

Table: BLBLI: beta-lactam/beta-lactam inhibitor combination. AG: aminoglycosides. SII: susceptible-intermediate isolates. RI: resistant isolates. LD: low dose, ≤6 million IU/day. HD: high dose, >6 millionIU/day.