populations and certain type of infections but the quality of the evidence supporting empirical combination antibiotic therapy is weak and does not include high quality randomised clinical trials (RCTs).
Objectives: To assess benefits and harms of empirical mono- *vs.* combination antibiotic therapy in adult patients with severe sepsis in the intensive care unit (ICU).
Methods: We performed a systematic review according to the Cochrane Collaboration methodology, including meta-analysis, risk of bias assessment and trial sequential analysis (TSA). We included RCTs assessing empirical mono-antibiotic therapy versus a combination of two or more antibiotics in adult ICU patients with severe sepsis. We exclusively assessed patient-important outcomes, including mortality. Two reviewers independently evaluated studies for inclusion, extracted data, and assessed risk of bias. Risk ratios (RRs) with 95 % confidence intervals (CIs) were estimated and the risk of random errors was assessed by TSA.
Results: Thirteen RCTs ($n = 2,633$) were included; all were judged as having high risk of bias. There was no difference in mortality (RR 1.11, 95 % CI 0.95 - 1.29; $p = 0.19$) or in any other patient-important outcomes between mono- *vs.* combination therapy. In TSA of mortality, the Z-curve reached the futility area, indicating that a 20 % relative risk difference in mortality may be excluded between the two groups. For the other outcomes, TSA indicated lack of data and high risk of random errors.
Conclusions: This systematic review of RCTs with meta-analysis and TSA demonstrated no differences in mortality or other patient-important outcomes between empirical mono- *vs.* combination antibiotic therapy in adult ICU patients with severe sepsis. The quantity and quality of data was low without firm evidence for benefit or harm of combination therapy.

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De-escalation, antimicrobial adequacy and culture positivity in septic patients in a middle income country: observational study

R.B. Moraes[1,2], F.K. Borges[3], J.A.V. Guillen[3], W.J.C. Zabaletta[3], PICS- HCPA: Programa Intrahospitalar de Combate à Sepse do Hospital de Clínicas de Porto Alegre
[1]Hospital de Clínicas de Porto Alegre, Intensive Care Unit, Porto Alegre, Brazil; [2]Hospital Femina Grupo Hopsitalar Conceição, Intensive Care, Porto Alegre, Brazil; [3]Hospital de Clínicas de Porto Alegre, Internal Medicine, Porto Alegre, Brazil
Correspondence: R.B. Moraes – Hospital de Clínicas de Porto Alegre, Intensive Care Unit, Porto Alegre, Brazil
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Introduction: De-escalation antibiotic in sepsis is associated with reduced costs and bacterial resistance. However, often it is not done.
Objectives: We designed this study with the primary objective to evaluate the prevalence of de-escalation in patients with severe sepsis or septic shock in an academic public hospital in south Brazil. Secondarily we evaluated antibiotic adequacy and cultures positivity.
Methods: We analyzed prevalence of de-escalation, antibiotic adequacy and culture positivity in severe sepsis and septic shock patients in an Intensive Care Unit.
Results: Of the 224 patients included, de-escalation could have been performed in 29 % of cases (66 patients), but was implemented in only 19 % of cases (44 patients). Among patients who received de-escalation, half was for antimicrobial spectrum narrowing. The mortality was not different between patients with or without de-escalation (56.8 % versus 56.1 %, p = 0.999). Empirical antimicrobial therapy was adequate in 89 % of cases. Pathogens were isolate in 30 % of all cultures and 26.3 % of blood cultures.
Conclusion: The rate of empiric antibiotic adequacy was high, reflecting active institutional policy of monitoring the epidemiological profile and institutional protocols of antimicrobial use. However, the antimicrobial de-escalation could have been higher than reported. De-escalation did not impact mortality. There are few data in the literature regarding the care of severe sepsis patients in developing countries. This data can contribute to adequate treatment in this scenario.

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Impact of amikacin pharmacokinetic/pharmacodynamic parameters on clinical outcome of gram-negative infection in critically ill patients

J. Ruiz-Ramos[1], P. Ramirez[1], M.R. Marqués-Miñana[2], E. Villarreal[1], M. Gordon[1], M. Sosa[1], P. Concha[1], A. Castellanos[1], R. Menendez[3]
[1]Hospital Universitari i Politècnic la Fe, Intensive Care Unit, Valencia, Spain; [2]Hospital Universitari i Politècnic la Fe, Pharmacy, Valencia, Spain; [3]Hospital Universitari i Politècnic la Fe, Pneumology, Valencia, Spain
Correspondence: P. Ramirez – Hospital Universitari i Politècnic la Fe, Intensive Care Unit, Valencia, Spain
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Introduction: Despite recent advances, appropriate initial amikacin dose in critically ill patients is still challenging. Relationship between pharmacokinetic/pharmacodynamic (pk/pD) parameter peak concentration (Cmax)/minimum inhibitory concentration (MIC) in critically ill patients is not clear.
Objectives: We assessed the impact of amikacin pharmacokinetic and pharmacodynamic parameters on clinical and microbiological outcome in these patients.
Methods: Observational prospective study. Adult patients (>18 years) admitted to an intensive care unit (ICU) with a gram negative documented infection and treatment with amikacin were included (Study period: September 2014 - April 2015). Amikacin blood samples were taken 24 to 72 hours after treatment started. Amikacin concentration were determined using Indiko® (Thermo Fisher Scientific), and drug adjustment were based on the recommendations given by the Pharmacokinetics Unit (Pharmacy Service).
Clinical response, defined as sign and symptoms presented at the moment of infection diagnosis (fever, chest radiography alteration, infection biomarkers elevation and hemodynamic instability), was evaluated. Ji-square and U-Mann Whitney test were used to compare results between treatment responders and not-responders.
Results: 49 patients were included [(Mean age: 56.0 (SD:2.0) years; Median APACHE-II: 22 (IQT: 22–27)]. 25 patients (51.0 %) presented mechanical ventilated infection, 10(20,4 %) catheter-related infections and 5(10.2 %) sepsis without clear focus. Mean bacterial isolated were *K pneumoniae* (40.8 %), *E Cloacae* (18.3 %) and *P aeruginosa* (17.5 %). Mean initial dose was 1150 mg (SD: 45,9)/day, equivalent to 15.8 (0.6) mg/kg/day. With that dose, 40 patients (83,7 %) reached a Cmax/MIC value higher than 8. Final treatment response was higher for those patients with amikacin Cmax/MIC value >8 (61,0 % vs 12,5 %; p = 0.028). No significant differences were reached in