promising potential source of new drug for treating infections caused by these clinical pathogens.

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Randomized equivalence trial of amoxicillin versus placebo for fast breathing pneumonia (RETAPP)

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Background: Fast breathing pneumonia or isolated tachypnea in children, is presumed to be mostly viral in origin. WHO guidelines recommend 3 days of amoxicillin therapy for all children with fast breathing pneumonia in resource limited settings. The recommendations have arisen largely out of hospital studies where the spectrum of disease is more severe. High quality clinical trial evidence to challenge or support the continued use of antibiotics, in low-resource community settings is lacking.

Methods & Materials: A community based randomized double blinded placebo-controlled non-inferiority trial is being conducted at primary healthcare centres located in two low income squatter settlements of Karachi, Pakistan. Children aged 2-59 months with WHO defined fast breathing pneumonia are included if they have no danger signs, SaO2 ≥ 90% on pulse oximetry, absence of use of antibiotics in last 48 hours, no bulging fontanels, pedal edema, asthma, tuberculosis or congenital heart disease. Children are being randomized to receive either 3 days of oral Amoxicillin (standard) or matching placebo (intervention), with 1215 children to be enrolled in each arm. Primary outcome is the difference in treatment failure rates between the two groups, defined as a new clinical sign based on preset definitions indicating illness progression or mortality on day 0, 1, 2 or 3 of therapy.

Results: From September 2014 till August 2015, a total of 19,363 children were triaged. Among these, 11,161 (58%) presented with cough or difficulty in breathing. 2,216 (20%) met the inclusion criteria i.e. have history of cough for less than two weeks and have tachypnea. About 40% of all fast breathing under 5 years occurs in babies 2-11 months of age. Of these children with fast breathing, 1056 children have been enrolled so far. The overall treatment failure is 3% and no mortality.

Conclusion: The overall rates of treatment failure and relapse in fast breathing pneumonia are low. The trial results will strengthen the evidence to support or refute the use of antibiotics in WHO-IMCI management of pneumonia. Findings will be generalizable to resource limited settings with low HIV and malaria prevalence and Hib and Pneumococcal vaccines in their national immunization plan.

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Colistin PK-PD (pharmacokinetic-pharmacodynamics) in Indian patients

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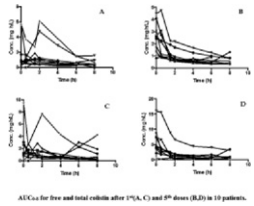
Background: A renewed interest in the usage of polymyxins has been observed, as they are the only treatment option left for multidrug resistant (MDR) and pan-drug resistant (PDR) pathogens like *Acinetobacter baumannii.* However, knowledge of the pharmacokinetics (PK) and pharmacodynamics (PD) of polymyxins is limited, resulting in inappropriate dosing, potential toxicity and development of resistance. We planned to conduct this prospective PK-PD study of intravenously administered colistin in Indian patients with MDR Gram-negative infections to estimate the levels of both total and free colistin.

Methods & Materials: This was a prospective PK-PD study of intravenously administered colistin in ten patients with MDR Gram-negative infections. The recommended systemic dose of prodrug, colistin methanesulfonate (CMS) was given as 4–6 mg/kg per day as a short-term infusion (for 1 hour) or 1–2 million IU/day in three divided doses (12,500 IU/1mg of CMS). Highly sensitive UHPLC-MS/SRM method was developed and validated to quantify free and total colistin from human sera. Correlation between the predictor variables like AUC/MIC ratio was performed using GraphPadInstat ver. 6 for Mac version 10.10.1 (GraphPad Software, San Diego CA: www.graphpad.com).

Results: The area under the plasma concentration-versus-time curve over 8 hrs (AUC_{0-8}) for free and total colistin ranged after 5th dose from 28.2 to 126 mg*Ÿh/liter and 25.8 to 404.9 mg*Ÿh/l respectively. All the follow up blood cultures were sterile and majority of the patients survived.



AUC (0-8) for free and total colistin after 1st(A, C) and 5th doses (B,D) in 10 patients

Conclusion: This is the first Indian study where free colistin levels were also estimated. The desired colistin levels to be effective without giving the loading dose were achieved in these Indian

patients. This study challenges the pharmacokinetic rationale for a loading dose similar to a study byGregoire N, *et al* (2014).

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The sensitivity to antibiotics of nosocomial strains of acinetobacter baumanii isolated in the tertiary hospitals in the Central Kazakhstan

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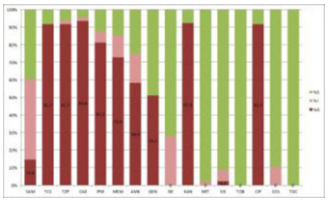
Background: Acinetobacter baumanii are one of main bacterial pathogen caused nosocomial infection according International Guidelines of Infection Control (2015). Last 4 years the part of nosocomial infection caused by Acinetobacter baumanii are dramaticaly grows.

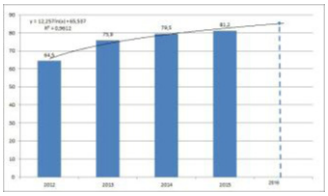
Methods & Materials: In the multicenter study 200 strains of Acinetobacter baumanii were collected in period 2012-2015yy. Strains were collected in 3 tertiary hospitals in the Central Kazakhstan. All strains were identified by MALDI-TOF mass-spectrometry and typed by PCR detection of OXA-51 carbapenemase as A.baumanii specific label. The sensitivity testing were by micro dilution methods with CLSI criteria using. The OXA-23 and OXA-40 carabapenemases genes detection made by PCR with commercial kits (Interlab Service, Russia). The statistical analysis (MIC90, average MIC, 95% Confidential Interval) was made by WhoNet 6.2 database.

Results: All isolated strains are resistance to main part of antimicrobial drug (pic. 1). During fourth years period the resistance to carbapenems were increased: to imipenem 64,5%; 95%CI 45,5-80,2 (2012 year) to 81,2; 95%CI 66,8-90,5 (2015 year). The resistance growth by logarithmyc depence (y = 12,257ln(x) + 65,537; R^2 = 0,9612). The testing of general linear hypothesis in regression situation for logarithmic model can predict level of resistance in 2016 at over 85% (pic.2). The dynamic of increasing to meropenem was the same and changed from 61.3% (2012) to 84,5% (2015y). In all cases of resistance to carbapenems the gene blaOXA-23 carbapenemase was detected. The quantitavive characteristics of sensitivity to antimicrobials are present in table 1. The high part of studied strains were sensetivity to aminoglycosides: netilmycin (97,9%), sisomycin (91,3%), tobramycin (100%) and colistine (89,6%) and tigecycline (100%). However all preparations mentioned above are not registered in Kazakhstan so can't using for treatment infections caused A.baumanii.

Conclusion: The resistance to carbapenems in the fourth tertiary hospitals in the Central Kazakhstan are increased during 2012-2015yy. The major cases of resistance to beta-lactams were linked with OXA-23 carbapenemase production. Some part of antibiotics (netilmycin, sisomycin, tobramycin, colistin and tigecycline) has high activity against studied nosocomial strain of A.baumanii but this drug not registered in Kazakhstan.

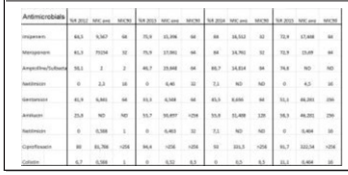


Pic 1. The resistance to antibiotics of nosocomial srtains A.baumanii isolated in the Central Kazakhstan's tertiary hospitals (2015).



Pic 2. The dynamic of the resistance to imipenem of nosocomial strains A.baumanii isolated in Central Kazakhstan's tertiary hospitals (2012-2015yy).

Table 1
The sensitivity to antimicrobials of nosocomial strains A.baumanii isolated in fourth tertiary hospitals in the Central Kazakhstan (2012-2015yy.)



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Computer assisted rational design and synthesis of some novel 2,4-di-substitued thiazole derivatives and their metal complexes (copper, cobalt, and nickel) as inhibitor of bacterial metabolic enzymes

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Background: Recent clinical reports have highlighted the increasing occurrence of methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE) and other antibiotic-resistant human pathogenic microorganisms. Transition metal complexes of heterocyclic moieties or/with Schiff's base components have been reported to show promising nucleolytic activity. In an effort to develop newer generation low molecular