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P1-BT01

Comparing the effects of inappropriate empirical antibiotic therapy on mortality in adults with community-onset gram-positive and gram-negative bacteremia

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Background: Early administration of appropriate antimicrobials has been correlated with a better prognosis in bacteremic patients, but a research highlighting a comparison of the adverse impact of inappropriate empirical antibiotic therapy between patient with Gram-positive and Gram-negative bacteremia is insufficient.

Methods: In a retrospective cohort study, adults with community-onset monomicrobial bacteremia during the 6-year period were enrolled. Clinical information was retrieved from medical records, using a predetermined case record form. Antimicrobial susceptibility was determined by the disk diffusion method, based on performance standards of the Clinical Laboratory Standard Institute in 2016. A propensity-score-matched analysis was performed to control for the baseline characteristics at bacteremia onset between the Gram-positive and Gram-negative groups. The propensity score was calculated by the independent predictors of 28-day crude mortality recognized by a multivariable logistic regression model.

Results: The total 2,053 adults (Gram-positive, 566 patients and Gram-negative, 1,487) presenting with community-onset monomicrobial bacteremia between the six-year period were recruited. Bacteremia severity (a Pitt bacteremia score) at onset and initial manifestation was different between two groups. On the basis of seven independent predictors of 28-day mortality recognized by the multivariate regression, 566 of the 1,487 patients in the Gram-negative group were matched to 566 patients in the Gram-positive group with the closest propensity scores. After appropriate propensity-score matching, no significant differences were observed in baseline characteristics and patient outcomes between the two groups, in terms of age, bacteremia severity, major comorbidities, comorbidity severity, and 28-day mortality.

Consequently, the Kaplan–Meier curves both revealed a significant difference between appropriate and inappropriate empirical antibiotic therapy in matched Gram-negative (odds ratio [OR], 2.49; $P < 0.001$) and Gram-positive (OR, 1.81; $P = 0.02$) groups.

Conclusion: a great adverse impact of inappropriate empirical therapy on patient survival and different clinical manifestation was observed in patients with community-onset Gram-negative bacteremia.

P1-BT02

Clinical predictors for *Stenotrophomonas maltophilia* bacteremia in adult patients with hematologic malignancy

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Background: *Stenotrophomonas maltophilia* (SM) has emerged as an important nosocomial pathogen with high morbidity and mortality. Because of its unique antimicrobial susceptibility pattern, appropriate antimicrobial therapy for SM bacteremia is still challenging, especially in immunocompromised patients. The present study was performed to evaluate clinical features of SM bacteremia in patients with hematologic malignancy and to assess clinical predictors of SM bacteremia in this population.

Methods: A case-control study was performed at a tertiary hospital from 2006 through 2016. Case patients were defined as SM bacteremia (SMB) in patients with hematologic malignancy. Date-, and location-matched controls were selected from patients with gram-negative bacteremia (GNB) other than SMB.

Results: A total of 118 cases with SMB were identified and compared to 118 controls. While pneumonia was the most common source of SMB, catheter-related infection was most common in the controls. The overall 30-day mortality rate of cases with SMB was significantly higher than that of the controls (61.0% and 32.2%, $P < 0.01$). A multivariable analysis showed that mixed infection with other organisms, previous SM isolation, the number of different antibiotics used ≥ 3 , and breakthrough bacteremia during carbapenem therapy were significantly associated with SMB (All P -values < 0.01). Previous use of SMX/TMP had a negative association with SMB ($P < 0.01$).

Conclusion: Our data suggest that SM is becoming a significant pathogen in patients with hematologic malignancy, in association with increased use of antimicrobial agents including carbapenems. Several clinical predictors for SMB can be used for appropriate antimicrobial therapy in patients with suspected GNB.

Keywords: *Stenotrophomonas maltophilia*, Hematologic Malignancy, Bacteremia, Predictor.

P1-BT03**Effect of aromatic compound metabolism on chloramphenicol influx in *Acinetobacter baumannii***

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Background: The increase in prevalence of *Acinetobacter baumannii* and its resistance to commercial antimicrobial agents are serious worldwide problems. Treatment of MDR bacteria by chloramphenicol (CAM) alone might cause serious health problem due to its known toxicity to humans. In this regard, new strategies using antibiotic adjuvants might be helpful to reduce the administration of CAM doses. The aim of this study is to demonstrate that CAM has a synergistic effect with 4-hydroxybenzaldehyde (4-HBA) against *A. baumannii* and this effect is associated with protocatechuate transporter that uptake CAM into the cytoplasmic membrane.

Methods: The checkerboard assay was performed to investigate synergistic effect of 4-HBA with CAM. To explore the mechanism underlying the synergistic effect of CAM and 4-HBA, microarray analyses were performed on *A. baumannii* cells treated with CAM, 4-HBA and CAM plus 4-HBA. Highly expressed genes in the microarray analysis were further investigated using mutation and quantitative RT-PCR. The rate of [¹⁴C]-CAM transport was measured by ¹⁴C-CAM isotope.

Results: Bacterial metabolism modulated by environmental chemicals could alter antibiotic susceptibility. 4-hydroxybenzaldehyde (4-HBA), which cannot support the growth of *A. baumannii*, exhibited synergism only with amphenicol antibiotics including CAM and thiamphenicol. Interestingly, this synergistic effect was not observed with other growth-supporting, structurally similar compounds such as 4-hydroxybenzoate. Transcriptomic analysis demonstrated that genes involved in protocatechuate metabolism (*pca* genes), osmotic stress (*bet* genes) were significantly up-regulated by 4-HBA and CAM treatment. The ¹⁴C-labeled CAM influx was lower in a *pcaK1* (encoding a transporter of protocatechuate) deletion mutant and was higher in the *pcaK1* over-expressing cells relative to that in the wild type upon 4-HBA treatment. The amount of 4-HBA in the culture supernatant was, however, unaffected during the test conditions, validating that it was not metabolized by the bacteria. CAM resistant *A. baumannii* cells derived by serial passages through CAM-amended media exhibited lower level of *pcaK1* gene expression.

Conclusion: The expression of the protocatechuate operon and osmotic stress genes in *A. baumannii* were enhanced by 4-HBA, which led to increase uptake of CAM.

P1-BT04**Study of bacteriuria in pregnant women and determination of their antibiotic susceptibility patterns**

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Aim: Urinary Tract Infection (UTI) is one of the most frequently encountered problems owing to significant number of patients needing hospitalization during pregnancy. In pregnant women the incidence of UTI can be as high as 8%. The aims of this study were isolation of pathogenic bacteria from urine culture of pregnant women and determination of their antibiotic sensitivity patterns.

Methods: In this study, midstream urine samples from 139 pregnant women with gestation age ranging between 6 and 38

weeks referred to Obstetrics and Gynecology clinic of Sina hospital, Ahvaz, Iran, were collected. The samples were cultured on Macconkey and Blood agar by calibrated loop method and after overnight incubation at 37°C, standard colony count were performed, which the colony count of 100,000 CFU/ml or more were considered as serious bacteriuria. The isolates were simultaneously identified using conventional biochemical tests. The antibiotic susceptibility pattern was determined as recommendation of CLSI.

Results: From 139 urine samples, 29 (20.9%) were culture positive and colony count of more than 100,000 CFU/ml. Among them 23 (79.3%) were gram negative and 6 (20.7%) were gram positive bacteria. The most predominant isolate was *Escherichia coli* 19 (65.5%), followed by *Staphylococcus aureus* 4 (13.8%), and the lowest rate was belong to *Enterobacter* with one case (3.4%).

Based on the results of microscopic urine examination, 7 (24.1%) of samples revealed the presence of pus cells, and leukocyturia were observed in 11 cases (37.9%). The highest antibiotics sensitivity among gram negative isolates were seen against ceftazidime, ceftriaxone and cefotaxime, while they showed high resistance to amoxicillin and amoxicillin-clavulonic acid.

Conclusion: Based on overall results, the rate of bacteriuria in examined pregnant women were 20.9% with the common causes of *E. coli* and *Staphylococcus aureus*. The most effective antibiotics for most bacterial isolates were cefotaxime, ceftazidime, ciprofloxacin and nitrofurantoin respectively. So it is recommended that routine microbiological analysis and antibiotic sensitivity test of urine samples of pregnant women be carried out before the administration of the drugs for the treatment and management of UTIs to avoid antibiotics resistance.

Keywords: Bacteriuria, pregnant women, colony count, antibiotic susceptibility, *E. coli*

P1-BT05**Type VI secretion system regulated by RpoN in *Proteus mirabilis***

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Background: *Proteus mirabilis* is a common human pathogen causing urinary tract infections (UTIs), especially in patients with indwelling urinary catheters. Type VI secretion systems (T6SS) are known to contribute to bacterial pathogenicity by exerting toxic effects on host cells or competing bacterial species and are involved in a broad variety of functions such as biofilm formation and stress sensing. The regulation of *P. mirabilis* T6SS remains unclear. Recently, our transcriptome analysis revealed *P. mirabilis* T6SS was regulated by RpoN.

Methods: We first identified one T6SS main structure operon and four Hcp/VgrG effector operons in *P. mirabilis* N2 by sequence specific RT and then PCR. The regulation of four Hcp/VgrG effector operons by RpoN was confirmed by real-time RT-PCR and the promoter reporter assay. We investigated if RpoN can bind directly to T6SS promoter region by a DNaseI footprinting assay. Overexpression of the effector toxin was performed to disclose its function. The growth predominance test and killing assay were used to know the competition between wild type and *rpoN* mutant. We constructed *vipAB* (genes of T6SS sheath) mutant to confirm the regulator-mediated killing of T6SS.

Results: RpoN positively regulated T6SS by binding directly to the promoter regions of four Hcp/VgrG effector operons and thus regulated the expression of the downstream effector toxin. Overexpression of the effector toxin in wild-type *P. mirabilis* resulted in increased killing of *rpoN* mutant and *E. coli*. Accordingly, the growth predominance test and killing assay demonstrated that

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