357. Pulmonary infections and sepsis

3201 Late-breaking abstract: Effects of oleic acid on pulmonary morphofunctional and biochemical variables in experimental sepsis

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Corticosteroids can improve clinical outcome in patients with pneumonia. However, little is known about the effects of corticosteroids on systemic cytokine levels in these patients or which patients benefit most from corticosteroid therapy. Hospitalized, non-ICU/non-CMV patients with CAP were randomly assigned to a 4-day course of placebo (5 mg once a day) or placebo. Serum levels of IL-1Ra, IL-6, IL-8, IL-10, IL-17, TNF-α, INF-γ, MIP and MCP were measured at various time-points during hospital stay. We enrolled 304 patients. The median levels of IL-6, MCP, TNF-α, IL-8, and IL-1ra, all were significantly lower (p < 0.01) on day 2 in the dexamethasone treated patients compared to the placebo treated patients. In patients with an atypical bacterium, IL-1ra (p < 0.01), IL-6 (p < 0.01), IL-10 (p=0.06) and MCP (p=0.03) decreased faster in the dexamethasone group compared to placebo, in pneumococcal pneumonia only MCP (p=0.07) and TNF-α (p=0.50) decreased faster.

When IL-6 and IL-8 and MCP, being the most prominent proinflammatory cytokines were combined, patients who had all three cytokines above a predefined cut-off point benefited most from dexamethasone therapy. In the dexamethasone group only 2 patients (8.3%) died, while in the placebo group 8 patients (47%) died (p=0.003).

Conclusion: Proinflammatory cytokines and chemokines decreased more rapidly in dexamethasone treated patients compared to placebo treated patients. This effect was most evident in patients with an atypical bacterium. In patients with highest cytokine response, dexamethasone showed a reduction in mortality and ICU admittance.

3204 Impact of bronchoalveolar lavage (BAL) multiplex PCR with DNA macroarray based diagnosis on outcomes of severe pneumonia in ICU

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Objective: To evaluate BAL multiplex PCR with DNA macroarray (Syndrome Evaluation System, SES), Xcyton Diagnostics Pvt. Ltd., India in etiological diagnosis of severe pneumonia and its impact on outcomes.

Method: Bronchoscopic BAL in 25 (27 episodes) adult patients with severe pneumonia was tested by conventional culture (CC) and SES. Empirical antibiotics were modified based on the results. Index infection, ICU, hospital and 30 day outcomes were compared with matched controls.

Results: BAL was obtained from 25 (27 episodes) study patients [mean±SD age 61±18.3 yrs] and 27 control patients [age 60±14.3 yrs]. There was no significant difference in the age (p=0.044), APACHE IV score (74±27 vs. 76±62.2; p=0.8) and predicted mortality (29.4±22.3 vs. 26.9±21.2; p=0.017). ICU length of stay (LOS) (p=0.49) and hospital LOS (p=0.73) was not between the groups. Mechanical ventilation was required for 26 episodes in study and 25 in controls.

In the study arm all BAL were positive by SES, 9 were sterile by CC and 18 were positive by both methods. In SES missed 4 organisms picked up by CC. In controls 7/27 BAL were sterile by CC. In the study arm there was significantly less time to antibiotic modification (p=0.08) based on SES (31.8±4.4 hrs) as compared to CC (including Gram stain and colony morphology) (52.8±11.7 hrs). Observed 30 days mortality was 15/27 (study) and 13/27 (control). Index infection cure rates (p=1) and ICU (p=0.27), hospital (p=0.49) and 30 day (p=0.57) mortality were not significantly different in the two groups.

Conclusions: Multiplex PCR (SES) helps in early modification of empirical therapy but shows no impact on severe pneumonia outcome.

3205 Hyaluronic infusion improves survival in endotoxemic rats

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Background: It has been proposed that Hyaluronan (HA) acts as a vehicle for cytokines due to the strong negative charge on its surface. We hypothesized that HA would function like a cytokine scavenger, reducing inflammatory signaling cascade leading to improved survival in endotoxemia.

Methods: Endotoxin (Salmonella, 10 mg/kg) or an equal amount of 0.9% NaCl (NS) was injected into the jugular vein of rats. HA (1600 kDa, 0.35%) or NS was given 0.5 ml/h for 3 h as compared to CC (including Gram stain and colony morphology) (52.8±11.7 hrs). Observed 30 days mortality was 15/27 (study) and 13/27 (control). Index infection cure rates (p=1) and ICU (p=0.27), hospital (p=0.49) and 30 day (p=0.57) mortality were not significantly different in the two groups.

Conclusions: Haemorrhagic shock and induced bleeding is a frequently observed complication in patients with severe trauma.

3203 Reduction of the systemic inflammatory response in patients with CAP treated with corticosteroids improves clinical outcome and reduces mortality and ICU admittance

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Corticosteroids can improve clinical outcome in patients with pneumonia. However, little is known about the effects of corticosteroids on systemic cytokine levels in these patients or which patients benefit most from corticosteroid therapy. Hospitalized, non-ICU/non-CMV patients with CAP were randomly assigned to a 4-day course of placebo (5 mg once a day) or placebo. Serum levels of IL-1Ra, IL-6, IL-8, IL-10, IL-17, TNF-α, INF-γ, MIP and MCP were measured at various time-points during hospital stay. We enrolled 304 patients. The median levels of IL-6, MCP, TNF-α, IL-8, and IL-1ra, all were significantly lower (p < 0.01) on day 2 in the dexamethasone treated patients compared to the placebo treated patients. In patients with an atypical bacterium, IL-1ra (p < 0.01), IL-6 (p < 0.01), IL-10 (p=0.06) and MCP (p=0.03) decreased faster in the dexamethasone group compared to placebo, in pneumococcal pneumonia only MCP (p=0.07) and TNF-α (p=0.50) decreased faster.

When IL-6 and IL-8 and MCP, being the most prominent proinflammatory cytokines were combined, patients who had all three cytokines above a predefined cut-off point benefited most from dexamethasone therapy. In the dexamethasone group only 2 patients (8.3%) died, while in the placebo group 8 patients (47%) died (p=0.003).

Conclusion: Proinflammatory cytokines and chemokines decreased more rapidly in dexamethasone treated patients compared to placebo treated patients. This effect was most evident in patients with an atypical bacterium. In patients with highest cytokine response, dexamethasone showed a reduction in mortality and ICU admittance.

3202 Inflammatory biomarkers in predicting ICU admission of severe community-acquired pneumonia (CAP)

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Introduction: Increased inflammation is related with severity and outcome in CAP. We tested the relationship between inflammatory response, prediction for ICU admission, delayed ICU admission, and outcome in patients with CAP.

Methods: We prospectively assessed 627 ward and 58 ICU patients (36 direct and 22 delayed ICU admission), determined serum levels of C-reactive protein (CRP), Procalcitonin, TNF-alpha, IL-1, IL-6, IL-8 and IL-10 at admission, and assessed the prediction for ICU admission of biomarkers and the IDSA/ATS guidelines criteria for severe CAP.

Results: Procalcitonin (p=0.001), CRP (p=0.005), TNF-alpha (p=0.042) and IL-6 (p=0.003) levels were higher in ICU patients, but the IDSA/ATS guidelines minor criteria predicted better ICU admission (OR 12.0, 95% CI 5.1-28.2, p < 0.001).

No patient with >3 minor criteria and Procalcitonin levels < 0.35 mg/ml needed ICU admission, compared with 14 (23%) with levels above this optimal cutoff (p=0.032). In initially-ward patients, Procalcitonin (p=0.012) and CRP (p=0.039) predicted subsequent ICU transfer, adjusted for age, co-morbidities and PSI risk class. Despite initially in wards, 14 (64%) patients with delayed ICU admission had criteria for severe CAP at admission, compared with 73 (12%) ward patients (p<0.001).

Conclusion: Although the IDSA/ATS guidelines minor criteria identified patients needing ICU admission better than biomarkers, lower levels of Procalcitonin discouraged ICU admission in those with minor criteria. Correctly applying these guidelines would reduce delayed ICU admission.

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Significantly associated with the VAP PIRO score (p < 0.01) reduced in the HA treated groups compared to controls (total cell count, 9.2 × 10^5/ml vs. 6.1 × 10^5/ml; neutrophils, 21.8 × 10^5/ml vs. 0.2 × 10^5/ml, respectively). Serum cytokines of the animals surviving HA or NS infusion 4 h after LPS showed that TNF-alpha and MIP-2 were significantly (p < 0.01) lower in the HA treated groups compared to controls (70.7 vs. 120.3 pg/ml; 1500 vs. 3459 pg/ml, respectively).

Conclusion: Continuous infusion of hyaluronan, 1600 kDa, reduced BAL cell count and serum cytokines, and improved survival in the endotoxic rats.

3206 Multi organ failure in severe sepsis patients followed at intensive care unit: Risk factors

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Aim: We aimed to detect risk factors for mortality and multi organ failure (MOF) for patients with severe sepsis and MOF in intensive care unit (ICU).

Method-material: Retrospective data collection and prognostic cohort study. Between January 2009-March 2010 686 patients received mechanical ventilation in a tertiary university hospital. The study period and fifty two (7.58%) developed VAP. Mortality for VAP was significantly (p < 0.001) lower in the HA treated groups compared to controls (70.7 vs. 120.3 pg/ml; 1500 vs. 3459 pg/ml, respectively).

Conclusion: Continuous infusion of hyaluronan, 1600 kDa, reduced BAL cell count and serum cytokines, and improved survival in the endotoxic rats.

Results: 347 patients (232 males) with severe sepsis were involved. Fortythree (12.4%) developed MOF and overall mortality rate was 14.9% (n=52). Presence of resistant pathogen, shock, total parenteral nutrition (TPN) and high APACHE II score were found to be risk factors for MOF (p<0.015 Odds ratio (OR) 3.47 confidence interval (CI): 1.27-9.47, p<0.000, OR 3.08, CI 1.13-8.39, p<0.005, OR 1.10, CI 1.04-1.18, respectively). Risk factors for overall mortality were presence of nosocomial infection, high 3rd day SOFA score, presence of shock, sedation and TPN (p<0.005, OR 3.39, CI 1.45-7.93; p<0.000, OR 1.51, CI 1.27-1.81; p<0.014, OR 3.24, CI 1.27-8.25; p<0.003, OR 3.64, CI 1.54-8.58; p<0.000, OR 3.38, CI 1.51-7.57, respectively).

Conclusion: In severe sepsis patients who need ICU follow up, in addition to known sepsis protocols, rational use of antibiotics and application of hospital acquired infection control programmes will further reduce MOF and mortality.

3207 Prediction of clinical severity and outcome of ventilator-associated pneumonia in a tertiary hospital using the VAP PIRO scoring system

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Background: Management and decision-making in ventilator-associated pneumonia (VAP) was commonly guided by diagnostic tools, until a recent study validated a severity assessment tool for prognostication.

Objective: To determine if VAP PIRO Scoring System can predict mortality risk and multi organ failure (MOF) for patients with severe sepsis and MOF in intensive care unit (ICU).

Methods: A prospective, observational study was performed including 52 patients with severe sepsis who needed mechanical ventilation. APACHE II was used as a severity assessment tool for prognostication. Risk factors and mortality risk factors in patients with and without MOF.

Results: 686 patients received mechanical ventilation during the study period and fifty two (7.58%) developed VAP. Mortality for VAP was significantly (p < 0.01) lower in the HA treated groups compared to controls (70.7 vs. 120.3 pg/ml; 1500 vs. 3459 pg/ml, respectively).

Conclusion: Significant association with the VAP PIRO score (p < 0.01) reduced in the HA treated groups compared to controls (total cell count, 9.2 × 10^5/ml vs. 6.1 × 10^5/ml; neutrophils, 21.8 × 10^5/ml vs. 0.2 × 10^5/ml, respectively). Serum cytokines of the animals surviving HA or NS infusion 4 h after LPS showed that TNF-alpha and MIP-2 were significantly (p < 0.01) lower in the HA treated groups compared to controls (70.7 vs. 120.3 pg/ml; 1500 vs. 3459 pg/ml, respectively).

Conclusion: Continuous infusion of hyaluronan, 1600 kDa, reduced BAL cell count and serum cytokines, and improved survival in the endotoxic rats.

3208 De-escalation therapy in ventilator acquired pneumonia (VAP):

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Objective: To evaluate the new strategy (De-Escalation of Antibiotics) for eight days. All patients were followed up and assessed clinically and by CPIS (Clinical Pulmonary Infection Score), at starting therapy and the days (three, eight, and fourteen)

Results: The proportions of patients with late and early VAP in Group A were 56.25%, 43.75% and Group B were 54.34%, 45.65%. The mortality rate was significantly higher in late and early VAP in both groups. In Group B the CPIS and clinical improvement was noticed and statistically significant in day eight, comparing to Group A (39.13%, 28.12% respectively). We studied the type of bacteria and its resistance to antibiotics, the proportion of Gram-negative almost consists two thirds in both groups with no difference in distribution of germ. The mortality rate in Group A was (65.62%), 56.52% Respectively The difference was statistically significant.

Conclusion: The (De-Escalation of antibiotics) was possible and safe with diminu- tion of mortality, the amounts of antibiotcs used and a shorter stay in the ICU.