MCP-1 and the Development of Pediatric ARDS

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BACKGROUND: Up to 50% of children admitted to the pediatric intensive care unit require mechanical ventilation, and 6% of ventilated patients meet criteria for the most severe form of lung injury, pediatric acute respiratory distress syndrome (PARDS). Monocyte Chemoattractant Protein 1 (MCP-1) is a chemokine that recruits monocytes to sites of inflammation. Pediatric studies have shown a relationship between elevated MCP-1 levels, severity of pneumonia, and mortality in patients with influenza infections.

OBJECTIVES: In ventilated patients admitted to the Ann & Robert H. Lurie Children's Hospital of Chicago Pediatric Intensive Care Unit (PICU), we investigated the relationship between peak MCP-1 levels in the first 72 hours of invasive mechanical ventilation and the presence or absence of PARDS at 48-72 hours after ventilation.

MATERIALS/METHODS: Prospectively collected specimens from patients admitted to the PICU who consented to enrollment in the PICU biobank were used for analysis. Oxygenation saturation index (OSI), oxygenation index (OI), the presence of PARDS, and pediatric logistic organ dysfunction score-2 (PELOD-2) were calculated for each subject. For eligible samples, a ProcartaPlex Custom 17-plex Luminex Assay was used to calculate mean fluorescence intensity of MCP-1 levels. We performed a Mann-Whitney U test as well as a logistic regression model to assess the relationship between MCP-1 levels and the presence or absence of PARDS. Secondary analyses investigated the relationship between MCP-1 levels and the presence of moderate or severe PARDS, peak OSI, and infectious status.

RESULTS: There were 129 subjects enrolled in the PICU Biobank, and 46 subjects met inclusion criteria with a plasma sample obtained within the first 72 hours of mechanical ventilation. The mortality rate in the cohort was 17%. Of the 46 subjects, there were eight (17%) with mild PARDS, seven (15%) with moderate PARDS, three (7%) with severe PARDS and twenty-eight (61%) patients who did not meet criteria for PARDS. A Mann-Whitney U test revealed a statistically significant difference in MCP-1 levels in subjects with and without PARDS ($p=0.001$). A logistic regression model showed a statistically significant relationship between MCP-1 levels and the presence of PARDS ($P=0.004$), which remained statistically significant when controlling for peak PELOD-2 score ($P=0.021$). A Mann-Whitney U test did not show a difference between MCP-1 levels and the presence of moderate or severe PARDS ($p=0.074$). A linear regression showed no relationship between MCP-1 levels and peak OSI ($p=0.271$). There was no relationship between MCP-1 levels and a positive respiratory culture ($p=0.345$) or a positive respiratory viral panel ($p=0.197$).

CONCLUSION: Peak MCP-1 levels in the first 72 hours of ventilation correlate with the presence of PARDS. MCP-1 levels did not correlate with the presence of a viral or bacterial infection. This implicates MCP-1 in the development of PARDS and suggests that there are multiple pathways that trigger elevated MCP-1 levels in pediatric patients.