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ANTI-INFLAMMATORY TREATMENT PARTIALLY ALLEVIATES DYSFUNCTION OF PULMONARY SURFACTANT IN MECONIUM-INDUCED ACUTE LUNG INJURY

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Dysfunction of pulmonary surfactant in meconium aspiration syndrome (MAS) is caused by inflammation, oxidation, lung edema and other factors. Various anti-inflammatory drugs have been used in the treatment of MAS, diminishing the above mentioned changes. Whereas little is known about direct consequences of the treatment on surfactant, this study was performed to evaluate reversibility of surfactant function after anti-inflammatory treatment in experimental MAS model. Oxygen-ventilated rabbits were intratracheally given suspension of meconium (25 mg/ml, 4 ml/kg; Mec) or saline (Sal). Thirty minutes later, meconium-instilled animals were given intratracheally budesonide (0.25 mg/kg, Mec+Bud), intravenously dexamethasone (0.5 mg/kg, Mec+Dex), aminophylline (2 mg/kg, Mec+Amin), olprinone (0.2 mg/kg, Mec+Olp), or N-acetylcysteine (10 mg/kg, Mec+Acc). Except the last two, all the mentioned drugs were given also in the second dose 2 hours after the first dose. Animals were sacrificed 5 hours after the first treatment dose. Healthy animals, not ventilated with oxygen and sacrificed at the beginning of experiment served as controls (Contr). At the end of experiments, bronchoalveolar lavage (BAL) of the left lung was performed and differential leukocyte count in the sediment was estimated. Supernatant of BAL was adjusted to a concentration of 0.5 mg phospholipids/ml. Surface properties of surfactant were evaluated by capillary surfactometer and were expressed by initial pressure necessary to transport the sample through the capillary, and by percentage of total time, for which the capillary was open (capillary patency). Right lung was used to determine lung edema by wet/dry (W/D) weight ratio. Due to oxygen ventilation, lung edema formation increased ($p<0.01$), capillary patency shortened ($P<0.001$) and initial pressure slightly increased ($p>0.05$) in Sal vs. Contr group. The changes were more pronounced after meconium instillation, when higher W/D ratio, increased neutrophil count in BAL fluid, shorter capillary patency and higher initial pressure were found in Mec vs. both Sal and Contr groups (all $p<0.001$). Anti-inflammatory treatment decreased W/D ratio (all $p<0.001$, 0.01 or 0.05) and reduced neutrophils in BAL fluid compared to non-treated Mec group ($p<0.01$ for Mec+Bud, $p<0.05$ for Mec+Dex and Mec+Acc, $p>0.05$ for Mec+Amin and Mec+Olp). As a result, treatment slightly improved the surface properties of surfactant, however, the only significant improvement was observed after dexamethasone ($p<0.01$ for initial pressure in Mec+Dex group, all other $p>0.05$). Negative correlations between capillary patency and W/D ratio resp. neutrophils in BAL fluid ($r= -0.630$, $p<0.001$, resp. $r= -0.752$, $p<0.001$), and positive correlations between initial pressure and W/D ratio resp. neutrophils in BAL fluid ($r=0.498$, $p<0.001$, resp. $r=0.612$, $p<0.001$) were found. In conclusion, anti-inflammatory agents reduced lung edema and

neutrophil influx into the lung and partially reversed the surfactant dysfunction in meconium-induced acute lung injury, with dexamethasone as a superior surfactant-enhancing agent.

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