

COMBINATION OF BUDESONIDE AND AMINOPHYLLINE IN EXPERIMENTAL MECONIUM ASPIRATION SYNDROME

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Introduction: High-dose glucocorticoids and methylxanthines have improved lung function in meconium-instilled animals, but influenced several cardiovascular parameters. Considering their additive effects we have supposed that combination of low-dose budesonide and aminophylline may keep favorable effects on lung function in reduced adverse effects. **Methods:** Adult rabbits were intratracheally instilled 4 ml/kg of human meconium (25 mg/ml) or saline (n=7). When respiratory failure developed, meconium-instilled animals were treated at 0.5 and 2.5 h after meconium instillation by intravenous aminophylline (1.0 mg/kg, n=7), or by budesonide (0.125 mg/kg) administered intratracheally using inpulsion regime of high-frequency jet ventilation 5 min later followed by intravenous aminophylline (1.0 mg/kg, n=8), or animals were left without treatment (n=7). All animals were further oxygen-ventilated for additional 5 hours after the first dose of treatment. Blood gases, respiratory and cardiovascular parameters and white blood cell count (WBC) were regularly evaluated. At the end of experiments, animals were killed by an overdose of anesthetics and trachea and lungs were excised. Left lungs were saline-lavaged and differential WBC in the sediment was estimated. Right lungs were used to determine lung edema by wet/dry weight ratio and oxidative damage by estimation of thiobarbituric acid-reactive substances, dityrosine and lysine-lipid peroxidation products. In addition, strips from trachea and right lungs were used for measurement of *in vitro* airway reactivity to histamine. **Results:** Although aminophylline improved some respiratory parameters, budesonide combined with aminophylline more effectively reduced right-to-left pulmonary shunts and improved gas exchange, with no significant cardiovascular effects. Combined treatment reduced lung edema and number of lung WBC (particularly neutrophils) to higher extent than aminophylline. Both treatments reduced peroxidation and *in vitro* airway reactivity to histamine, but these effects were slightly more pronounced after single aminophylline. **Conclusions:** Budesonide combined with aminophylline improved respiratory and several inflammatory parameters in meconium-instilled rabbits more effectively with less cardiovascular side effects than single aminophylline. However, no additive effect of budesonide to aminophylline was observed in lipid and protein peroxidation and *in vitro* airway reactivity compared with aminophylline.

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