

## EFFECTS OF LOW-DOSE AND HIGH-DOSE AMINOPHYLLINE ON LUNG FUNCTION IN A MODEL OF MECONIUM ASPIRATION SYNDROME

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**Introduction:** Methylxanthine derivatives may be beneficial in the treatment of meconium aspiration syndrome. Since there is no information on appropriate dosing, this study compared effects of high-dose and low-dose aminophylline on lung function of meconium-instilled rabbits. **Methods:** Artificially ventilated rabbits (2.6±0.3 kg) received intratracheally a suspension of human meconium (4 ml/kg, 25 mg/ml). When respiratory failure developed, animals intravenously received aminophylline at high-dose (HD, 2.0 mg/kg, n=8) or at low-dose (LD, 1.0 mg/kg, n=7) at 0.5 and 2.5 h after meconium instillation, or were left without treatment (n=7). All animals were further oxygen-ventilated for additional 5 h after the first dose of treatment and respiratory parameters, blood gases, and white blood cell count (WBC) were 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:** HD-aminophylline significantly improved gas exchange, reduced ventilatory pressures and right-to-left pulmonary shunts and decreased edema formation, and number of lung neutrophils compared to non-treated group. LD-aminophylline enhanced oxygenation, diminished ventilatory pressures, and pulmonary shunts, but to lower extent than HD-aminophylline, and failed to reduce significantly the lung edema and number of lung neutrophils. Both HD- and LD-aminophylline decreased oxidative damage to lung proteins and lipids, with more pronounced effect of HD-aminophylline on TBARS and of LD-aminophylline on dityrosine levels. Tracheal reactivity to histamine significantly decreased after HD-aminophylline, while lung tissue reactivity was more reduced after LD-aminophylline. **Conclusions:** HD-aminophylline enhanced pulmonary function, diminished lung edema and several inflammation-related parameters in meconium-instilled rabbits more effectively than LD-aminophylline. However, stronger response of LD-aminophylline on lung tissue reactivity and dityrosine suggests participation of other anti-inflammatory mechanisms on the level of lung parenchyma.

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