

SINGLE-DOSE *VERSUS* TWO-DOSE DEXAMETHASONE EFFECTS ON LUNG INFLAMMATION AND AIRWAY REACTIVITY IN MECONIUM-INSTILLED RABBITS

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Introduction: A two dose regimen of corticosteroid dexamethasone might alleviate meconium-induced acute lung injury more effectively than single dose.

Material and methods: Air-ventilated adult rabbits received intratracheally 4 ml/kg of saline (Sal, n=5) or human meconium (25 mg/ml). From this moment, animals were oxygen-ventilated. When respiratory failure developed, meconium-instilled rabbits received one dose of dexamethasone (0.5 mg/kg i.v.) 0.5 h after meconium instillation (Mec+Dex1, n=7), two doses of dexamethasone (each of 0.5 mg/kg i.v.) 0.5 h and 2.5 h after meconium instillation (Mec+Dex2, n=8), or were left without treatment (Mec, n=8). All animals were ventilated for additional 5 h after the first dose of treatment. Total and differential white blood cell (WBC) counts were evaluated regularly. Right lungs were used to determine airway reactivity by in vitro method, lung edema by wet/dry weight ratio, and oxidative damage to lipids and proteins by estimation of thiobarbituric acid-reactive substances, tyrosine and lysine in lung homogenate. Left lungs were saline-lavaged and differential WBC was estimated in BAL sediment.

Results: Two doses of dexamethasone effectively diminished meconium-induced lung edema, tracheal hyperreactivity to histamine, neutrophil count in BAL associated with higher WBC and neutrophil counts in the blood as well as oxidative modifications of proteins and lipids in lung homogenate compared to Mec group (all $P < 0.01$ or $P < 0.001$). Single-dose dexamethasone reduced lung edema, BAL neutrophils and tracheal hyperreactivity to histamine, but to lower extent than two-dose dexamethasone, and failed to prevent oxidative lung injury.

Conclusions: Two-dose dexamethasone reduced lung edema, inflammation and airway hyperreactivity in meconium-instilled rabbits more effectively than single-dose treatment.

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