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Caffeine Prevents Hyperoxia-Induced Functional and Structural Lung Damage in Preterm Rabbits.

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Abstract

BACKGROUND: Caffeine is a commonly used drug for apnea of prematurity. It may, however, also have a beneficial effect on bronchopulmonary dysplasia (BPD), which is the most common complication of extreme preterm birth.

OBJECTIVES: To study the inflammatory, structural and functional effects of caffeine in an animal model of BPD.

METHODS: Preterm New Zealand-Dendermonde rabbits (gestational day 28; term 31) were randomized to three groups: normoxia-placebo (N-P), hyperoxia-placebo (H-P) and hyperoxia-caffeine (H-C). Lung function was assessed on postnatal day 5, along with airway morphometry, vascular morphometry and a score observing airway inflammation.

RESULTS: Caffeine improved lung function by increasing lung volume [mean displaced volume N-P: 40.1 ± 6 ml/kg, H-P: 27.8 ± 8 ml/kg and H-C: 34.4 ± 7 ml/kg ($p < 0.05$); total lung capacity: N-P: 1.17 ± 0.1 ml, H-P: 0.67 ± 0.1 ml and H-C: 1.1 ± 0.1 ml ($p < 0.05$)], decreasing tissue damping [N-P: 2.7 ± 0.3 cm H2O/ml, H-P: 4.6 ± 0.6 cm H2O/ml and H-C: 3.2 ± 0.4 cm H2O/ml ($p < 0.05$)], elastance [N-P: 9.3 ± 2.4 cm H2O/ml, H-P: 19.2 ± 7.4 cm H2O/ml and H-C: 10.7 ± 2 cm H2O/ml ($p < 0.05$)] and compliance [N-P: 0.06 ± 0.01 cm H2O/ml, H-P: 0.054 ± 0.01 cm H2O/ml and H-C: 0.07 ± 0.013 cm H2O/ml ($p < 0.05$)]. Caffeine also improved histology by decreasing alveolar size [linear intercepts; N-P: 83.6 ± 1.7, H-P: 82.9 ± 1.6 and H-C: 67.3 ± 1.4 ($p < 0.05$)], increasing radial alveolar count (N-P: 6.6 ± 0.5, H-P: 5.7 ± 0.6 and H-C: 7.05 ± 0.5) and decreasing the acute inflammation score [N-P: 0.3 ± 0.1, H-P: 0.5 ± 0.1 and H-C: 0.4 ± 0.1 ($p < 0.05$)].

CONCLUSION: In preterm rabbits, caffeine reduces the functional, architectural and inflammatory pulmonary changes induced by hyperoxia in the lung.