PROTECTIVE ROLE OF ADENOSINE MONOPHOSPHATE-ACTIVATED PROTEIN KINASE ALPHA IN HYPEROXIA-INDUCED EXPERIMENTAL BRONCHOPULMONARY DYSPLASIA

AHMED L ELSAIE[1], Binoy Shivanna[2], Sharada H Gowda[2], Nidhy P Varghese[3], Roberto Barrios[4], Renuka Menon[2], Amrit Shrestha[2]

[1] Baylor College of Medicine, Department of Pediatrics, Neonatology

[2] Baylor College of Medicine, Pediatrics, Neonatology

[3] Baylor College of Medicine , Pediatrics, Pulmonology

[4] Houston Methodist, Clinical Pathology, clinical pathology

Background: Bronchopulmonary dysplasia (BPD) is the most common chronic lung disease of preterm infants and hyperoxia is a major risk factor for this disease. Histopathologically, BPD is characterized by alveolar simplification (fewer and larger alveoli). Our studies showed that hyperoxia exposure increases lung adenosine monophosphate-activated protein kinase alpha (AMPKα) activation in neonatal mice. Whether this alteration is a compensatory or contributory phenomenon in hyperoxia-induced experimental BPD is unknown. Therefore, we hypothesized that lung AMPKα activation protects against hyperoxia-induced experimental BPD in neonatal mice.

Materials/Methods: C57BL/6J wild-type (WT) male and female mice pups were housed in air (21% FiO2, normoxia) or 70% O2 (hyperoxia) for 14 d while they are injected intraperitoneally (i.p.) with the AMPKα agonist, aminoimidazole-4-carboxamide ribonucleotide (AICAR), or the vehicle daily through postnatal days (PND) 1 to 14. Lung tissues were harvested on PND7 or PND14 to determine lung AMPKα activation and development, respectively. AMPKα activation was determined by immunoblotting, whereas alveolar development was evaluated by radial alveolar count (RAC) and mean linear intercept (MLI).

Results: At PND7, AICAR administration increased phosphorylated AMPKα protein levels, indicating that the compound activated AMPKα in our experimental conditions. Hyperoxia-exposed mice had a decrease in RAC and an increase in MLI indicating that their alveoli were fewer in number and larger in diameter, respectively, when compared with normoxia-exposed mice. Interestingly, AICAR treated mice had increased alveolar development at basal conditions (normoxia exposure). Further, AICAR treatment decreased hyperoxia-induced alveolar simplification.

Conclusions: These findings support our hypothesis that AMPKα signaling mitigates hyperoxia-induced experimental BPD in neonatal mice. We propose that AMPKα is a potential target for the development of new therapies for BPD.