GROWTH AND DIFFERENTIATION FACTOR 15 (GDF15) IN PRETERM INFANTS AND ITS RELATION TO BRONCHOPULMONARY DYSPLASIA – A PILOT STUDY

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Background: Bronchopulmonary dysplasia (BPD) is one of the most common morbidities among surviving premature infants. A gap in BPD research is the lack of methods to identify infants at higher risk of developing BPD. Earlier identification will enable targeted postnatal interventions to prevent or attenuate its severity. GDF15 is a stress-responsive cytokine and a divergent member of the TGF-β superfamily. Its expression increases under stress conditions, including inflammation, hyperoxia, and senescence. GDF15 levels increase in cardiopulmonary disorders like congestive heart failure, pulmonary hypertension, and acute respiratory distress syndrome. The circulatory GDF15 levels in preterm infants have not been studied, and its role as a biomarker in evolving lung injury is unknown. Our hypothesis is that in preterm infants, postnatal lung injury is associated with increased serum GDF15 levels.

Materials/Methods: Infants born between 23- to 36- weeks gestation were enrolled in the study (n=44). Following parental consent, scavenged blood samples were retrieved at five-time points: (day of life one (DOL 1), DOL 7, DOL 14, 4th week of life, and postmenstrual age 36 weeks) (n=83/135). The samples were stored at -80ºC until analysis. GDF15 levels were measured using the human GDF15 ELISA kit DGDF150 (R&D Systems). Statistical analysis was performed using simple linear regression and mixed-effects linear models. Significance was identified when $P<0.05$.

Results: The serum GDF15 levels at DOL 1 (n=26) showed that for each additional week of gestational age at birth, the level decreased by 334.2 pg/mL ($r=-0.479$, $P=0.016$). After controlling for gestational age at birth, the longitudinal predicted GDF15 level decreased by 113.2 pg/mL ($P<0.001$) for each additional DOL. Higher circulatory GDF15 levels were associated with longer mechanical ventilation time ($P=0.024$), higher oxygen requirement ($P<0.001$), and longer respiratory support need ($P<0.001$). In infants born at ≤30 week gestation (n=13), the change in serum GDF15 levels over time was not significantly different for infants with versus without BPD (n=7 vs. n=6, $P=0.273$).

Conclusions: In preterm infants, the baseline serum GDF15 levels, at DOL 1 are higher in infants born at lower gestation. The circulatory GDF15 levels trended down over time postnatally in all preterm infants. Infants who required higher and longer respiratory support had higher GDF15 levels. The change in serum GDF15 level over time was not significantly different for infants with versus without BPD.

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