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Plasma KL-6 as a potential biomarker for BPD in neonates

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PURPOSE / OBJECTIVES

Bronchopulmonary dysplasia (BPD) is a chronic inflammatory lung disease of very-low-birth-weight (VLBW) preterm infants, associated with arrested lung development and a need for supplemental oxygen. The incidence of BPD stays extremely high during the last years as a result of improved survival of VLBW infants. BPD is often difficult to early diagnose and prevent due to the lack of good biomarkers for the identification of infants at risk.

Krebs von den Lungen (KL-6) is a glycoprotein mainly expressed and secreted by bronchial epithelial cells and type II pneumocytes, whose expression correlates with the presence and severity of several chronic lung diseases.

We aimed to establish if there is any difference in plasma KL-6 in VLBW infants below 28 gestational weeks, divided into groups depending on the presence and severity of BPD.

MATERIALS & METHODS

For a period of one year are determined the plasma levels of KL-6 on day 7 and day 14 after birth in infants below 28 gestational weeks. We analyze 35 infants. Patients are divided into two groups: group A (15 infants) – without or with mild BPD; group B (20 infants) – with moderate or severe BPD. Laboratory method is Chemiluminescent Enzyme Immunoassay (CLEIA). Lumipulse G KL-6 is an assay system including a set of immunoassay reagents, for the quantitative measurement of KL-6 in specimens based on CLEIA technology, by a two-step sandwich immunoassay method on the LUMIPULSE G System (FUJIREBIO). The Assay is fully automated. The measurement range of method is from 50 to 10000 U/mL. If the KL_6 concentration of a specimen exceeds 10000 u/mL, dilute using Specimen Diluent 1 and re-measure.

RESULTS

No differences in gestational age, weight, Apgar scores, the severity of Respiratory distress syndrome. The duration of mechanical ventilation and Oxygen therapy is longer in group B (infants with moderate and severe BPD). Two infants from group B with severe BPD have plasma KL-6 above 1000 U/mL at two weeks of life. The mean plasma level of KL-6 on day 7 in group A is 315 U/mL, while in group B is 337 U/mL. In group A we find a reduction of the biomarker on day 14 – mean level 199 U/mL, whereas in group B the mean levels of KL-6 increase – 498 U/mL, and this difference is statistically significant. Patients from group B with the most severe BPD have the highest levels of KL-6 on day 14th after birth. Except severe BPD, patients with the highest levels of KL-6 both on day 7 and day 14 have also severe chronic complications – Retinopathy of prematurity and Intraventricular hemorrhages.

KL-6 is preferentially expressed on alveolar type II cells in human lungs and is a marker of specific lung injury. Following alveolar injury, regenerating type II cells strongly express KL-6 antigen and this can lead to increased plasma KL-6 levels. Markedly increased KL-6 levels in plasma have been reported in patients with various interstitial lung diseases. The predictive characteristics of increased levels of KL-6 in serum and tracheal aspirate at an early age for the development of bronchopulmonary dysplasia (BPD) in pre-term infants, have been recognized.

Standard upper limits of serum KL-6 in a group of children with nonrespiratory disease are up 250 U/mL, or half the adult level. In healty adult donors the observed range is 118-627 U/mL.

RESULTS

Characteristic* Data are presented as average value within range in drackets or as number and % (in brackets)	**Group A /n=15/**	**Group B /n=20/**	**P**
Weight (g)	1060 (790-1550)	851 (600-1320)	**0,052**
GA	26,9 (26-27)	26,15 (24-27)	**0,192**
Percentage <26+0 wks GA	3 (20%)	4 (20%)	**1,000**
C-section, n (%)	6 (40%)	15 (75%)	**0,001**
Antenatal steroids	12 (80%)	14 (70%)	**0,092**
RDS III-IV	11 (73%)	19 (95%)	**0,009**
Mechanical ventilation (days)	7,8 +/- 6,3	28,9 +/- 16,3	**0,001**
O2-therapy (days)	26 +/- 19	59,5 +/- 43,4	**0,001**
KL-6 - day 7 (U/ml)	315 (190-447)	337 (179-574)	**0,098**
KL-6 - day 14 (U/ml)	199 (122-261)	498 (112-2021)	**0,001**

SUMMARY/CONCLUSION

Plasma KL-6 could be an early screening marker for the detection of infants at higher risk for developing BPD.

Increasing levels of the biomarker during the first two weeks of life as well as very high plasma levels of KL-6 are typical for infants that develop severe BPD.

KL-6 could be useful for the early detection and prevention of this chronic lung disease.

The laboratory method CLEIA Lumipulse G KL-6 has no interference in a study consistent with the guidelines in the CLSI Protocol EP7-A2 of free bilirubin up 18.7 mg/dl and conjugate bilirubin up 19,7 mg/mL