Plasma Neuronal Injury Marker Neurofilament in the First Days of Life in Preterm and Term born Infants

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BACKGROUND AND AIM

- Neurofilament (Nf) = proteins form the axonal skeleton
- Quantification of Nf proteins in the peripheral blood has been proposed in adults as biomarker for neuronal injury (1)
- Levels of Nf proteins in newborn infants are largely unknown
- Aim: To investigate Nf light chain (NfL) plasma concentrations in preterm and term born infants during the first days of life

METHODS

This prospective observational study was performed at the University Children’s Hospital Basel (UKBB). Neonates (n=203) with a median GA of 37.9 (IQR 31.9-39.4) weeks were included.

- Blood samples: 185 umbilical venous blood samples at birth and 39 venous blood samples at day of life (DOL) 3
- Plasma NfL was measured by a highly sensitive single molecule array (Simoa) assay

RESULTS I

The cohort was divided into a very preterm group (GA <32 weeks; n=52) and a moderate preterm and term (MPT) group (GA ≥32 weeks; n=151).

	Moderate Preterm and Term (≥32 weeks GA) n=151	Very preterm (<32 weeks GA) n=52
Neonatal characteristics		
GA (weeks)	38.3 (37.0-40.0)	30.1 (28.3-31.3)
BW (g)	3270 (2710-3630)	1360 (1063-1463)
Sex (male, %)	87 (57.6)	25 (48.1)
Brain damage (%)	1 (0.7)	10 (19.2)
O ₂ duration (days)	0	4 (1-15.8)
pH umbilical artery	7.30 (7.26-7.33)	7.32 (7.29-7.37)
NEC (%)	0	0
Sepsis (%)	0	11 (21.2)
5-min Apgar	9 (9-9)	7 (5.25-8)
Death (%)	0	6 (11.5)
Maternal characteristics		
Age (years)	32 (29-36)	33 (28.3-36.0)
Amniotic infection (%)	5 (3.3)	13 (25)
Preeclampsia (%)	16 (10.6)	20 (38.5)
PROM (%)	14 (9.3)	14 (26.9)
DM (%): Primary CS	76 (50.3)	26 (50)
Secondary CS	29 (19.2)	21 (40.4)
VD	46 (30.5)	5 (9.6)

The median plasma concentration of NfL at birth (18.2 pg/mL, IQR 12.8-30.8) was lower compared to DOL 3 (50.9 pg/mL, IQR 41.3-100.1, p<.001). NfL levels were higher in very preterm infants than in the MPT group at birth (median 32.5 pg/mL, n=47 vs. 15.3 pg/mL, n=138; p<.001), but not at DOL 3 (median 48.5 pg/mL, n=16 vs. 51.4 pg/mL, n=23; p=.668).

RESULTS II

NfL levels at birth significantly correlated with BW (R=-.403, p<.001, Figure 1), GA (R=-.271, p<.001), 5-min Apgar (R=-.295, p<.001) and oxygen duration (R=.333, p<.001).

Presence of preeclampsia (31.0 pg/mL vs. 16.2, p<.001) and sepsis (32.6 pg/mL vs. 17.85, p=.033) were associated with higher NfL levels.

In the MPT group NfL levels at birth were higher in infants delivered vaginally than by primary or secondary cesarean section (21.8 vs. 13.9 and 14.4 pg/mL; p=.002) (Figure 2).

Multivariable logistic regression analysis identified as independent predictors of NfL: BW (beta=-.297, p=.003), delivery mode (beta=.237, p=.001) and preeclampsia (beta=.183, p=.022).

CONCLUSION

Neonatal NfL levels correlate inversely with maturity and BW, increase during the first days of life and are influenced by maternal factors such as delivery mode and preeclampsia.

Reference
1: Yuan A, Rao MV, Veeranna, Nixon RA. Neurofilaments and Neurofilament Proteins in Health and Disease. Cold Spring Harbor perspectives in biology. 2017;9(4).