Early neonatal determinants and neurological outcome in the first three years of life of newborn undergoing hypothermic treatment: a single center prospective study

Letizia **Capasso**, Serena **Salomè** *, Maria **Vendemmia**, Valentina **Esposito**, Chiara **Colinet**, Alessia **Salatto**, Fiorentino **Grasso**, Giuseppina **Mansi**, Francesco **Raimondi**

Department of Neuroscience, Reproductive Science and Odontostomatology, University of Naples Federico II, Naples, Italy.

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Objective. Therapeutic hypothermia (TH) is the gold standard treatment for hypoxic-ischemic encephalopathy (IIE) affecting mortality and neuro-behavioral disability. The objective of this study was to identify early markers (in the first days of life) of subsequent neurological outcome in neonates undergoing TH in order to individualize the post neonatal follow-up and counselling with parents.

Materials and Methods. Neonates who received hypothermic treatment (according to the recommendations of the SIN 2012) from 2014 to 2021 at NICU "Federico II" were included in a register and followed prospectively for the first 3 years. Determinants of severity of clinical conditions in the first days of life were recorded (pattern of aEEG at enrollment and after hypothermic treatment, seizures, inotropic treatment, pathological MRI according to Okereafor). Such determinants were related to psychomotor development (Hammersmith and Griffiths tests) performed during the follow-up in the first 3 years of life by means of not parametric (Spearmann Rho coefficient) and linear regression analysis (level of significance set as $p < 0.05$).

Results. 38 infants were included in the register. The aEEG pattern at enrolment was correlated with neurological outcome as Hammersmith at 12 months (rs -0.412, $p = 0.026$); there was correlation between normalization of the aEEG within 72 h and neurological outcomes at 12 and 24 months (rs -0.551, $p = 0.008$; rs -0.551, $p = 0.008$, respectively). Seizures showed the best correlation with abnormal Griffith scales at 12 months (rs -0.634, $p = 0.000$); treatment with both dopamine and dobutamine had the stronger correlation with abnormal Hammersmith score at 12 (rs = 0.556, $p = 0.002$) and 24 months (rs = 0.490, $p = 0.021$); abnormal MR was the best predictor of psychomotor retardation at 24-months according to Griffith scales (rs 0.770, $p = 0.00$).

Conclusions. The failure of normalization of aEEG, seizures and pathological brain MRI are the main factors associated with an unfavorable long-term neurological outcome. Moreover, we showed that inotropics treatment during hypothermia may represent an early predictor of abnormal neurological long term outcome.