Semi-Mechanistic Model to Predict In-Hospital Natural Weight Changes in Term Neonates

Mélanie Wilbaux1*, Severin Kasser2, Sven Wellmann2, Chiara De Angelis3, Hanna Rickenbacher2, Noemi Klarer2, Johannes N. Van Den Anker1,4, Marc Pfister1,5

1Department of Paediatric Clinical Pharmacology, Paediatric Pharmacology and Pharmacometrics Research Center, University Children’s Hospital Basel (UKBB), Basel, Switzerland. 2Division of Neonatology, UKBB, Basel, Switzerland. 3Department of Pediatrics, San Gerardo Hospital, Monza, Italy. 4Division of Pediatric Clinical Pharmacology, Children’s National Health System, Washington, DC, USA. 5Quantitative Solutions LP, Menlo Park, CA, USA.

Objectives: The magnitude of physiological weight loss within the first days of life varies strongly among newborns and can reach high amounts resulting in serious long term complications. The objectives of this study were to develop a semi-mechanistic model to characterize natural weight changes during the first week of life and to quantify effects of key covariates on model parameters.

Methods: Longitudinal weight data and individual characteristics from 1335 healthy term breast-feeding neonates up to 10 days of life were available. A semi-mechanistic model was developed to characterize weight changes during these first days of life. A population analysis was performed with NONMEM7.3. Model selection was based on statistical criteria, goodness-of-fit plots and simulations. Covariate testing was performed utilizing a standard stepwise forward-backward covariate model building approach (SCM).

Results: Weight changes by time were described as a balance between weight gain rate (KIN) and weight loss rate (KOUT); Fig.1. KIN was modeled as an exponential function of time. KOUT was modeled with a saturable function to describe the initial loss of fluid followed by an exponential time-dependent increase. Gestational age had a positive effect on birth weight (WT0) and KIN. Gender was associated with WT0, with higher values in males. According to goodness-of-fit plots, weight changes were properly fitted. Visual predictive check demonstrated good predictive performance of the model; Fig.1.

Conclusions: We provide the first model describing the pattern of physiological weight changes in healthy breastfed neonates in the first days of life. Such a model could be a useful tool for clinicians to early detect neonates at risk for high amount of weight loss and consecutive morbidities.