Intergenerational transmission of sucralose and acesulfame-potassium from mothers to their infants via human milk: a pharmacokinetic study

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4.3 Statistical Design and Power

Sample Size

Given that the primary purpose of the proposed study is to evaluate sucralose and ace-K pharmacokinetics, formal sample size calculations were not performed. In order to conservatively account for 20% attrition, we will recruit a total of 48 lactating women and their infants in order to complete measurements on a planned sample of 40 mother-infant dyads.

Planned Analyses

The concentration-time profile of sucralose and ace-K in plasma and breast milk from mothers will analyzed by non-compartmental analysis (NCA)[35] and through a population pharmacokinetic approach using Pumas V1.0 (Baltimore, MD). Sucralose and ace-K concentrations (ng/mL) in plasma and breast milk will be first graphically explored and summarized descriptively. From the rich plasma and breast milk concentration-time data, NCA analysis will be performed to obtain the following PK parameters such as area under the curve (AUC), clearance, maximum concentration (C_{max}), time-to-maximum concentration (T_{max}) and terminal half-life ($T_{1/2}$). The milk-toplasma ratio (M:P) will be calculated for sucralose and ace-K. The population PK analysis of sucralose and aceK in mothers from plasma and breast milk will be performed using the non-linear mixed effect modeling approach.[36-38] Rich PK samples collected from mothers will be used to estimate the base PK model parameters and to characterize the effect of subject-specific prognostic factors (e.g., weight status, reported LCS consumption habits, overall dietary intake, body weight, maternal blood volume, age, sex, and race/ethnicity) to explain the between subject variability in the PK parameters. Plasma and breast-milk data will be analyzed together in the population PK analyses.

Using the sparse PK samples collected from the infants, a population PK analysis of sucralose and ace-K in infants will be performed, in combination with the robust maternal data.[39, 40] The PK model in mothers will serve as the starting point for developing the pediatric PK model. Using principles of allometry, the PK parameters will be scaled down to infants using body weight and age maturation factors for the PK parameters.[41] Additional infants' covariates will be evaluated in the combined PK model. The final population PK model for sucralose and ace-K in both mothers and infants will be evaluated and qualified using standard goodness of fit diagnostics and quantitative predictive check methods. The relative infant dose (RID) of sucralose and ace-K will be calculated as described in the FDA lactation guidance.[42] Given that blood volume differs in obese vs. lean individuals, adjustments for blood volume will be performed by calculating the total mass of sucralose or acesulfame-potassium in breast milk, as in our prior study.[7]