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Indomethacin Exposure is Associated with Birthweight in Extremely Preterm Infants: Non-standard Exposure with Standard Weight-Based Dosing

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☐ **Resident/Psychology Intern (≤ 1 month of dedicated research time)**
☐ **Resident/Ph.D/post graduate (> 1 month of dedicated research time)**
X Fellow

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IRB Number: 15090389

Describe role of Submitting/Presenting Trainee in this project (limit 150 words):

The trainee's role in this project was to process and analyze previously generated pharmacokinetic patient data. I calculated indomethacin exposure as AUC values in patients based on plasma concentrations measured at different timepoints across a 96-hour period. Association analysis was conducted between AUC values and several patient clinical and demographic endpoints.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background: Indomethacin (IND) is used in preterm infants for prophylaxis against intraventricular hemorrhage. It has a highly variable exposure between patients, with a risk of subtherapeutic or toxic levels from current dosing guidelines.

Objectives/Goal: The objective of this study was to measure IND concentrations in preterm infants and determine how patient characteristics are related to exposure.

Methods/Design: This was prospective cohort study of preterm infants enrolled at birth (n=10). They received intravenous IND administered in 3 doses of 0.1mg/kg over 96 hrs. Systemic IND was measured by plasma and dried blood spot. Urine samples were measured for IND and metabolites. Pearson correlation analysis was performed between IND AUC 0-96 hours, patient characteristics, and excretion endpoints.

Results: Results showed that IND $AUC_{0\text{-}96\ hrs}$ had a significant correlation with patient birthweight (BW) ($r=0.76$, $p=0.01$), as well as significant correlation between BW and percent drug recovered as unchanged IND in urine ($r=0.72$, $p=0.02$).

Conclusions: Current dosing regimens show higher levels of IND exposure for higher BW patients. The correlation between unchanged IND in urine and BW suggests that delayed metabolism of IND may contribute to the increased exposure. These results show that current IND dosing regimens are not achieving comparable exposure in preterm infants.