



COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar

Wednesday, March 2, 2022

4:00pm

2548 NUB or [Zoom](#)

“Midazolam Precision Pharmacotherapy in Neonates”

Presented by:



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Abstract: Midazolam is a benzodiazepine medication commonly used in the neonatal intensive care unit (NICU). It helps minimize the pain and stress associated with the many clinical procedures that these preterm infants need to undergo during their several months-long stay in NICU. To date, no clear concentration-effect relationship for midazolam has been found in neonate population and many research reported the PK-PD inconsistency of Midazolam. In this study, a SWATH capillary-LC-MS/MS analytical platform capable of simultaneously analyzing the compounds of interest and the whole plasma metabolomes of neonatal patients was developed. The neonate plasma samples from NICU were analyzed by this method. Midazolam PD information and patient demographic information were collected from electric health record. A two-compartment population PK model were successfully built with NONMEM to describe the pharmacokinetic profiles of midazolam and its two metabolites, 1-OH-Midazolam and 4-OH-Midazolam. Bodyweight, age, liver, and renal functions were incorporated in the PK model as covariates. PK parameters of midazolam and metabolites were estimated and compared with other reported studies. For the Midazolam PD response prediction, many machine learning classifiers were applied, and random forest classifiers achieved 83% accuracy and 98% precision. The relationship between midazolam PK and PD profiles are still under study. The findings of our research will help with the precision dosage of midazolam in neonates and improve the efficacy and safety of the drug.

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