

Evaluation of Pharmacokinetic Models for Infliximab Dosing for Crohn's Disease

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Introduction

Approximately 3 million people in the US are living with Crohn's Disease (CD), a disease characterized by chronic inflammation of the gastrointestinal tract. Treatment of CD includes biologic (monoclonal antibody) therapies that target pro-inflammatory pathways, like infliximab (anti-TNF). Initial response rates to infliximab are favorable, however, the annual loss of response rate is 12-15%. Drug concentrations below target is a major cause for infliximab failure in children, leading to a critical need for model-informed precision dosing (MIPD) to proactively maintain steroid-free remission

Aim

Test the performance (precision) of two pharmacokinetic (PK) models in a real-world pediatric Crohn's disease (CD) cohort.

Methods

This project is a retrospective, single-center study of pediatric CD subjects (n=105) starting infliximab. We included patients that were naïve to anti-TNF therapy and had at least one detectable drug concentration obtained during the first year of therapy.

Results

After analyzing available PK data focusing on only the last observed infliximab concentration and the models four covariates obtained in the last 182 days, the Minar PK model had a mean prediction error (MPE) of -5.4, mean absolute prediction error (MAPE) of 7.3, and 99% of the predicted concentrations falling +/-2.5 µg/mL within the actual concentration. . Adjusting the model to remove all undetectable drug levels in the cohort, the Minar model performed the best with MPE at -1.6, MAPE at 3.6, and 99% of predictions within the range. [MP1]

Conclusions

These results suggest that focusing model prediction on the last drug concentration and the most recent covariates of drug clearance may be more beneficial for drugs with a longer half-life like infliximab. Clinical decision support tools such as PK dashboards integrated into the electronic medical record can simplify precision dosing to automatically include these parameters that maximize concentration predictions.

Acknowledgements

This study was funded by NIH Grant T35 DK060444 through the Medical Student Summer Research Program (MSSRP) at the University of Cincinnati College of Medicine