Estimation of the Area-Under-the-Curve of Mycophenolic Acid using population pharmacokinetic and multi-linear regression models simultaneously.

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Mycophenolic Acid is an immunosuppressive drug administered to patients after organ transplantation in order to prevent rejection of the transplanted organ. Because of the complicated pharmacokinetics of this drug, as well as its side effects, patient exposure to the drug is often monitored [1]. The best available pharmacokinetic parameter to be monitored is the Area Under the Curve (AUC) on the plot of measured drug concentrations versus time, over the entire dosing interval. This parameter is tedious to achieve analytically, because it requires multiple blood draws and extended patient stay in the facility. Several methods exist, that allow estimation of AUC using fewer blood draws obtained in a shorter time interval, as compared to full dosing-time interval AUC [2].

In this study we simultaneously used two techniques: multi-linear regression models developed using SAS [2], and population-pharmacokinetic models developed using NONMEM [3] to estimate the AUC of mycophenolic acid in a semi-automated way.

We have created an *R* script that automatically loads patient data stored in a 'csv' file, prepares the dataset for *NONMEM* simulation and invokes a *NONMEM* run. Next, it loads the output from simulation and estimates the mycophenolic acid AUC in two ways: using an appropriate multi-linear regression equation and using `trapz` function (**caTools** library) from *NONMEM*-simulated concentrations. Finally, the script produces a graphical representation of the results of simulation, with embedded table of results (**plotrix** library) and all important patient characteristics. This is all performed without any user interaction neither with *R* nor with *NONMEM*.

Our script is suitable for use in any clinical toxicology laboratory by unqualified personnel, who would only be required to enter the data into a spreadsheet and run the script. The only prerequisite for this method to work is a *NONMEM* license. Our script provides the user with results of estimation of the Area Under the Curve using two methods, quickly and with minimum effort.

References

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