Poster

[P26-6] P26-6: Immunosuppressive drugs (5): Clinical practice

Chair: Hege Christensen, Norway

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[P26-6-3] Prediction of cyclosporine A blood concentration with voriconazole using Simcyp Simulator: case report

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Keywords: voriconazole, cyclosporine A, drug drug interaction, Simcyp Simulator, physiologically based pharmacokinetic model

Background

Voriconazole (VRCZ), a novel triazole antifungal agent, has a potent activity against a broad spectrum of yeasts and molds. VRCZ is metabolized by cytochrome P-450 (CYP) enzymes, namely CYP 2C9, 2C19 and 3A4. cyclosporine A (CyA) is metabolized by CYP3A4. VRCZ has been shown to interact with calcineurin inhibitors, this interaction has not been thoroughly examined. We experienced unexpected high concentration of CyA combined with VRCZ therapy. Therefore, it is important to predict the drug interaction of VRCZ with a variety of agents metabolized by these enzymes, including immunosuppressive agents, cyclosporine A.

Methods

A physiologically based pharmacokinetic (PBPK) modeling approach was employed to predict of the drug interaction in situations where VRCZ is administered with CyA. We predicted a pharmacokinetic change of the CyA using Simcyp Simulator Ver.15 with FULL PBPK Model (a Certara company). Estimated CyA concentration was compared with obtained value in the patients with aplastic anemia.

Results

The relative AUC value of CyA 300mg/day for VRCZ (400mg/day) was about 2.0. PBPK simulation showed a good predictive performance of estimating CyA concentration.

Conclusions

A prediction of pharmacokinetics is commonly difficult about the interaction of medicine causing inhibition and induction at the same time. Simcyp Simulator is useful TDM tool for various clinical situations.