Symposium

[S-12] S-12: TDM for central nervous system drugs

Chairs: Kiyofumi Yamada, Japan / Philip Nicholaou Patsalos, UK
Tue. Sep 26, 2017 10:30 AM - 12:00 PM Room E (1F)

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[S-12-4] Drug monitoring and dose individualisation of anti-epileptic drugs: a role for pharmacometrics

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Background

Pharmacokinetic (PK) models exist for most antiepileptic drugs (AEDs). They may be used in conjunction with data from therapeutic drug monitoring (TDM) to explore, with subsequent dosing adjustments to reach predefined target concentrations [1].To date, it is unknown to what degree applying such an approach is beneficial for epilepsy patients. Furthermore, it is unclear whether current empirical sampling approaches obtain optimal TDM information. Here we aim to determine if model-based dosing algorithms can be used to guide attainment of target exposure in patients.

Methods

Treatment scenarios were explored for 11 commonly used AEDs using clinical trial simulations (CTS) of steady-state concentrations (Css). For each AED, six dosing algorithm scenarios were considered: i. the patient population is treated with the same dose. ii. doses are personalised by individual clearances predicted by PK model covariates. iii-v. doses are individualised based on individual clearances estimated from one, two or three plasma samples from empirical timepoints, or from D-optimally designed timepoints (vi-viii). Target Css were set as reported in literature (Patsalos et al. 2008) and the ratio RTCss = observed Css / target Css was calculated. Efficient dosing algorithms should then show a median RTCss close to 1 (accuracy; RE%) and a narrow 95% predicted range (precision; CV%). A change of 5% RE or CV was considered relevant.

Results

Based on the selected scenarios, personalisation reduced CV for 2/11 AEDs (8.5%, 36.0%) in adults and 2/11 (5.9%,32.9%) in children. By contrast, individualisation using one plasma sample seems to reduce CV for 10/11 AEDs in adults (6.6-27.9%), and 9/11 in children (6.0-36.6%). The use of additional plasma samples resulted in minor improvements. Optimisation of sampling times did not result in improved dosing accuracy. RE was small in all scenarios.

Conclusions

In contrast to current clinical guidelines, our results show that patient demographic and clinical characteristics can be used in conjunction with PK models and TDM to individualise the treatment with antiepileptic drugs.