Poster

[P27-9] P27-9: Pharmacokinetics and PK/PD

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[P27-9-9] Quantitative prediction of drug removal rate by hemodialysis based on the permeation clearance of hemodialyzer

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Background

Drug removal rate by hemodialysis (f_d) is a crucial parameter to determine the optimal dosage for patients on hemodialysis, and volume of distribution (V_d) and plasma unbound fraction (f_U) are known to be important determining factors of f_d. However, the effect of hemodialysis conditions on f_d have not been examined quantitatively and remained to be elucidated. In this study, we aim to predict the f_d using pharmacokinetic parameters of drugs and hemodialysis conditions, especially focused on the permeation clearance of hemodialyzer membrane (KoA).

Methods

We selected 249 drugs which met the following criteria for the literature survey, 1) drugs listed in the “Drug Prescribing in Renal Failure” guidebook; 2) both V_d and f_U are available. Then, we searched the PubMed database for literatures in which the following information are reported, 1) hemodialysis clearance (CL_{HD}) or f_d; 2) blood and dialysate flow rate (Q_B and Q_D); 3) types of dialyzer material; 4) time of dialysis (T_{HD}). The predicted f_d values were calculated based on these parameters, and compared with the observed values. For calculation, the KoA value was fixed to 100 mL/min which was estimated from the pharmacokinetic data of iodine contrast agents in patients on hemodialysis.

Results

As the result of the literature survey, required parameters were available for 50 out of 249 drugs. Predicted f_d values were in good concordance with the reported values, and 28 and 38 drugs were within the 0.67~1.5 and 0.5~2 fold range of the predicted values, respectively. Interestingly, f_d values were overestimated when the CL_{HD} is assumed to be proportional to Q_B. This observation strongly suggest that the KoA is the rate limiting step of drug removal by hemodialysis.

Conclusions

The results of our study indicate that f_d values are predictable from pharmacokinetic parameters of drugs and condition of hemodialysis. These information is helpful to setting the optimal dosage for patients receiving hemodialysis.