Correspondence

Impact of SLCO4C1 Genotypes, Creatinine, and Spironolactone on Digoxin Population Pharmacokinetic Variables in Patients With Cardiac Insufficiency

Dear Dr Walson,

Thank you so much for your continued attention to our manuscript. We learned a lot from your letter.

Construction of the drug concentration-time curve for a drug that follows a 2-compartment model indicates that the curve may be divided into a distribution phase and an elimination phase. Because the population pharmacokinetic model was developed based on sparse data and limited observations were in the absorption and distribution phases, there are not enough data to develop the 2- and 3-compartment models. The objective function values of the 1-compartment model, 2-compartment model, and 3-compartment model are listed in Supplemental Table II (https://doi.org/10.1016/j.clinthera.2020.07.011). We compared the performances of different models and found that the 1-compartment model best fits our data. The 1-compartment model adequately described the data; however, the 2- and 3-compartment models failed to achieve successful convergence.

Routine therapeutic drug monitoring data were retrospectively collected. Reproducible and accurate quantitation is a requirement for clinical applications, and the results of interlaboratory evaluation and comparison demonstrate the reliability of this method. However, because of the limited resources of our laboratory, we have not been able to rule out the interference from both endogenous digoxin-like immunoreactive substances and exogenous medications. We asked the company (Siemens) to perform assay validation during the assay development, and the assay has been validated for its selectivity and potential cross-reactions with other compounds.

After continuous administration of digoxin and reaching steady state (at least 5 $t_{1/2}$s), 2 mL of venous blood was obtained from the patients. We did not interfere with clinical treatment, and the actual elapsed time since first dose was obtained from our hospital information system. Practitioners rarely use pharmacokinetic models to predict peripheral drug concentrations. In the clinical study, the target of the digoxin trough concentration was 0.8 to 2.0 ng/mL. In our future study, we will collect the rich pharmacokinetic data, prolong the sampling time, and consider peripheral drug concentrations.

We are very sorry for the mistakes in Table I. The initial doses were 0.125 mg or 0.25 mg. They should be corrected in our article.

DISCLOSURES

There is no conflict of interest to declare.

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https://doi.org/10.1016/j.clinthera.2021.02.005
DOIs of original articles: 10.1016/j.clinthera.2020.07.011, 10.1016/j.clinthera.2021.01.023