Abstract

The aim of this dissertation was to study the possibility of using pharmacokinetic parameters for individualized patient care. The thesis consists of four thematic areas: assessment of factors involved in drug pharmacokinetics changes in obese patients after bariatric surgery, implementation of therapeutic drug monitoring and dose adjustment of selected drugs based on these findings; pharmacokinetic analysis of rituximab levels in patients with glomerular diseases and proposal of individualized dosage regimen; review of pharmacokinetics of anticoagulants in patients undergoing plasmapheresis and therapeutic monitoring of anticoagulant therapy; and use of pharmacokinetic calculations to refine the analysis of non-adherence in patients with resistant hypertension.

Significant changes in concentrations of venlafaxine, quetiapine, trazodone, and carbamazepine were observed over a 6-month period after Roux-en-Y gastric bypass surgery, which were caused by the surgical procedure and changes in drug absorption, but also by alterations in carbamazepine levels and the influence of its induction potential. Repeated therapeutic monitoring of drugs with a narrow therapeutic window and high interaction potential leads to the necessary individualization of therapy in such complex situations and increases its safety and efficacy.

Analysis of rituximab levels in 185 patients indicated the need for dose adjustments in patients with membranous nephropathy, focal segmental glomerulosclerosis and lupus nephritis; the different pharmacokinetics in patients with these glomerulopathies is consistent with the described inferior therapeutic response to standard treatment regimens, as opposed to patients with ANCA-associated vasculitis or minimal glomerular disease. New dosing regimens with shortened administration intervals have been proposed for these difficult-to-treat diagnoses with high proteinuria.

After plasmapheresis was performed, we observed a loss of only 10% of the daily dose of apixaban, with plasma levels corresponding with the expected normal reference range, without bleeding or thrombotic complications during treatment; thus, this finding suggests the possibility of safe and effective anticoagulation with this drug even during this extracorporeal method.

Based on literature data and measured spironolactone and canrenone concentrations in a group of adherent patients, a two-step decision model for adherence assessment was developed and subsequently applied to a group of 71 patients with resistant hypertension. When pharmacokinetic principles were involved, twice as many non-adherent patients were detected compared to the traditional method of drug and/or metabolite detection in the sample. The method is thus particularly effective in the assessment of masked non-adherence.

Keywords:

adherence, dose optimization, personalized pharmacotherapy, pharmacokinetics, therapeutic drug monitoring