OATP1B1 and statin tolerability – from genetic variation to drug interactions

Project description:

Finding the right drug and dosage for the right patient remains challenging in many cases and interindividual drug responses are frequently observed. Especially, for the cholesterol-lowering treatment with statins it is known that more than 20% of patients experience statin-associated musculoskeletal symptoms (SAMS). This intolerance has been associated with impaired medication adherence, thereby increasing the risk of atherosclerotic cardiovascular diseases (ASCVD) in many patients. The organic anion transporting polypeptide 1B1 (OATP1B1), a liver uptake transporter, has been shown to influence systemic exposure to statins and thus their tolerability. Over 30% of the European population are carriers of *SLCO1B1* gene variants encoding for OATP1B1 with a significantly reduced or lacking activity phenotype. In addition, to a patient's genetic predisposition, also non-genetic factors such as their co-medication can affect statin tolerability (e.g., drug-drug-gene interactions). However, to date, it is not entirely clear which, how, and to what extent a combination of genetic and non-genetic factors should be considered in the evaluation of statin therapy.

Since OATP1B1 transports not only drugs but also endogenous substances such as coproporphyrins (CPs), the utility of measuring such substrates to determine the OATP1B1 phenotype is the subject of current research. In this master's thesis, you will analyze patient cases experiencing statin intolerance based on their pharmacogenetic profile, medication history and CP levels. You will test whether the measurement of endogenously formed CPs could be used as a biomarker to assess the individual OATP1B1 phenotype, as a result of drug-drug-gene interactions. Understanding the impact of OATP1B1 associated drug-drug-gene interactions in clinical practice may support the development of strategies for safe and tolerable statin therapy.

The experimental part of this work (incl. UHPLC-MS/MS and genotyping) will be performed in the Biopharmacy laboratory at the University of Basel.

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