Proposal for a Thematic Issue

Drug-induced nephrotoxicity and drug metabolism in renal failure

Aims and scope

Chronic kidney disease (CKD) leading to kidney failure is becoming a global public health problem. Acute kidney injury (AKI) is also a major kidney disease characterized by a rapid decline of renal function. Drug-induced nephrotoxicity is a contributing factor to AKI in 19-25% of critically ill patients. Drugs exert their toxic effects to cause nephrotoxicity by one or more common pathogenic mechanisms. The progressive loss of kidney function associated with CKD not only leads to impaired renal excretion of numerous drugs and their metabolites in the kidneys, but also alters the non-renal disposition of moieties that are extensively metabolized by the liver. Various alterations in activity of metabolic enzyme system have been reported in CKD models, for example, reductions in expression and activity of hepatic cytochrome P450 (CYP) enzymes including CYP3A1, CYP3A2, CYP2C11, and other enzymes such as N-acetyltransferases. What’s more, other mechanisms such as the dysregulation of drug transporter systems are involved in decreasing the clearance of drugs in renal failure. With the development of renal failure, the renal secretion of organic ions mediated by organic anion transporters (OATs) and organic cation transporters (OCTs) is decreased. Some organic anionic uremic toxins may directly inhibit the renal excretion of various drugs and endogenous organic acids by competitively inhibiting OATs.

The objective of this mini-thematic issue is to report recent studies about most common mechanisms of drug-induced nephrotoxicity and prevention strategies, the alterations of drug enzymes and transporters in the kidney and liver in renal failure, the potential model systems to predict drug efficacy, interactions, and drug-induced kidney injury in drug development.

Key words: chronic kidney disease, acute kidney injury, drug-induced nephrotoxicity, drug metabolism, organic transporters

Subtopic:
2. Metabolic enzyme system and transport pathways in kidney diseases
3. Hepatic drug metabolism in renal failure
4. Model systems to predict drug efficacy, interactions, and drug-induced nephrotoxicity

Schedule:
Manuscript submission deadline: December 2016
Peer review due: January 2017
Revisions due: March 2017
Notification of acceptance: April 2017
Publication: May 2017