Therapeutic drug monitoring in pediatrics

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Therapeutic drug monitoring consists in applying pharmacokinetic and pharmacodynamic assays to evaluate drug treatment in patients, in order to assure optimal therapeutic response. This approach could be particularly useful in pediatric patients, due to their peculiarities in drug disposition, associated with patients' growth and development (Zhao W and Jacqz-Aigrain E, 2011). Specific limitations of therapeutic drug monitoring in pediatric patients are associated with the need of additional evidence to demonstrate the usefulness of this approach and the need of collecting small volume of samples, on which to perform the pharmacological assays, particularly in very young patients. Polychemotherapy of acute lymphoblastic leukemia (ALL) constitutes a paradigm for successful application of therapeutic drug monitoring to improve outcomes (Pui and Evans, 2015). Pharmacokinetics of ALL currently involves monitoring drug concentrations of high-dose methotrexate during consolidation therapy, to select the appropriate dosage of leucovorin, in order to decrease methotrexate adverse effects. Improvements in current therapeutic drug monitoring of pediatric ALL could be obtained by considering methotrexate clearance instead of drug concentrations, in order to better predict methotrexate effects, and including monitoring of thiopurines during maintenance therapy, to improve compliance and outcomes. Pharmacodynamics of ALL therapy currently involves measuring molecularly the residual disease after induction therapy. Testing in vitro drug sensitivity of ALL cells at diagnosis, could optimize drug choice, particularly by avoiding or reducing ineffective drugs and could be useful in identifying molecular biomarkers for drug resistance (Paugh et al., 2015). Pharmacogenetics markers could also be helpful as surrogates of pharmacokinetics and pharmacodynamics evaluations to further improve therapy of pediatric ALL.

Zhao W and Jacqz-Aigrain E (2011). Handb Exp Pharmacol. 205,77-90.

Pui CH and Evans W (2013). Semin Hematol. 50,185-196.

Paugh et al. (2015). Nat Genet. 47,607-614.