

The drug dosing regimen should be based on the individual characteristics of the patient in order to increase drug effectiveness and to reduce adverse and toxic effects. However, such a personalized therapy requires the detailed knowledge of pharmacokinetics and pharmacodynamics of drugs and knowledge of inter-individual variability in response to the drug. The variability in drug response is mostly linked with genetic differences, however as important as those, are the environmental differences, drug interactions and health status of the patient. This aspect seems particularly important in the pediatric population treated in the intensive care units (PICU). The literature and our preliminary observation show a two-fold increase in dexmedetomidine clearance for infusion longer than 24 hr in intensive care patients. We hypothesized that its effect is driven by the induction of metabolism, although other causes like transient increase in cardiac output cannot be excluded. Therefore we would like to search for a mechanism explaining this phenomenon. During the realization of this project we will examine the influence of maturation, pharmacogenetics, metabolomics, and physiological (or pathophysiological) status of the patients on the pharmacokinetics and pharmacodynamics (PK/PD) of α_2 -adrenergic drugs (dexmedetomidine and clonidine) in a population of patients from the pediatric intensive care unit