

MUDr. Olga Matoušková – the dissertation theses
The influence of individual genetic predisposition to the
pharmacokinetics and pharmacodynamics of chosen opioids

ABSTRACT

Introduction: The aim of this thesis is to study the influence of polymorphism of CYP2D6 and MDR1 on the pharmacokinetics and pharmacodynamics of tramadol in healthy volunteers using measurement. A secondary objective is to evaluate these polymorphisms in relation to the analgesic efficacy and side effects of piritramide for acute postoperative pain.

Materials and methods: In two prospective work studying the influence of genetic predisposition on the pharmacokinetic and pharmacodynamic parameters of tramadol, we included a total of 90 healthy volunteers. Clinical studies on opioid analgesia and influence of genetic predisposition to the pharmaco-therapeutic effects and side effects in patients with acute postoperative pain, we included a total of 161 patients with acute postoperative pain. Polymorphism genotyping CYP2D6 and MDR1 gene we performed PCR - RFLP analysis, to determine concentrations of tramadol and metabolite, we used gas and liquid chromatography and pharmacodynamic effects of opioids was evaluated by pupilometric measurement and visual analogue scale.

Results and conclusion: Variability of the opioid effect is influenced by pharmacogenetic differences in metabolism caused by CYP2D6 gene polymorphism and the modifying effect of the efflux transporter P-glycoprotein. Polymorphism of CYP2D6 phenotype can be reliably especially relative concentrations of the ODT and tramadol levels 2,5 hours after drug administration and MDR1 polymorphisms of the sum of concentrations of ODT of urine in 2,5 hours after drug administration. Both polymorphisms can phenotype also using pupilometric measurements. Variability of analgesic effect of opioids and incidence of side effects in patients with acute postoperative pain affects gene polymorphism of CYP2D6 and MDR1.

Key words: tramadol, pupilometry, CYP2D6, MDR1, piritramide, acute postoperative pain, side effects, toxicological analysis