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Effect of *ABCB1* (*MDR1*) 3435C >T and 2677G >A,T polymorphisms and P-glycoprotein inhibitors on salivary digoxin secretion in congestive heart failure patients

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Abstract:
The aim of the present study was to evaluate the effects of *ABCB1* (*MDR1*) gene polymorphism on P-glycoprotein model substrate, i.e. digoxin, salivary secretion. The study was carried out in 77 patients diagnosed with congestive heart failure administered digoxin, who were subdivided into two groups: 1) co-administered P-glycoprotein inhibitors and 2) without any known P-glycoprotein inhibitors. The *ABCB1* 2677G >A,T and 3435C >T polymorphisms were evaluated using PCR-RFLP methods. Steady-state digoxin concentrations were measured in blood serum as well as in unstimulated and stimulated saliva using FPIA method. It was found that values of Pearson's coefficient were significantly higher in patients co-administered P-glycoprotein inhibitors in comparison with subjects who were not administered any inhibitor both for stimulated (Pearson's coefficient $r = 0.832$, $p < 0.01$) and unstimulated saliva ($r = 0.812$, $p < 0.01$). Evaluation of the impact of *ABCB1* 2677G >A,T and 3435C >T polymorphism on salivary digoxin secretion revealed significant differences in digoxin stimulated saliva/serum ratio between patients stratified by 2677G >A,T genotype (TT, TA > GT, GA > GG, $p < 0.01$). The results from the present study suggest that administration of P-glycoprotein inhibitors as well as *ABCB1* gene polymorphism may affect salivary digoxin secretion.

Key words:
ABCB1 polymorphism, P-glycoprotein, digoxin, salivary secretion