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Short communication

Impact of *ABCB1* (*MDR1*) gene polymorphism and P-glycoprotein inhibitors on digoxin serum concentration in congestive heart failure patients

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Abstract:
Digoxin, a drug of narrow therapeutic index, is a substrate for common transmembrane transporter, P-glycoprotein, encoded by *ABCB1* (*MDR1*) gene. It has been suggested that *ABCB1* polymorphism, as well as co-administration of P-glycoprotein inhibitors, may influence digoxin bioavailability. The aim of the present study was to evaluate the effects of *ABCB1* gene polymorphism and P-gp inhibitor co-administration on steady-state digoxin serum concentration in congestive heart failure patients. Digoxin concentrations as well as 3435C > T and 2677G > A,T *ABCB1* single nucleotide polymorphisms, were determined in 77 patients administered digoxin (0.25 mg daily) and methyldigoxin (0.50 mg daily), some of them co-medicated with known P-glycoprotein (Pgp) inhibitors. Significant differences were noted in digoxin serum concentrations ($C_{min,ss}$) between patients co-administered and not co-administered P-gp inhibitors: 0.868 ± 0.348 and 0.524 ± 0.281 for digoxin ($p < 0.002$), as well as 1.280 ± 0.524 and 0.908 ± 0.358 for methyldigoxin ($p < 0.02$), respectively. No influence of *ABCB1* 2677G > A,T and C3435C > T polymorphisms on digoxin concentration was noted. Although some of the previous studies have shown that digoxin pharmacokinetics might be affected by *ABCB1* genetic polymorphism, those modest changes are probably clinically irrelevant, and digoxin dose adjustment should include P-gp inhibitor co-administration rather than *ABCB1* genotyping.

Key words:
ABCB1 polymorphism, P-glycoprotein, digoxin, genetic polymorphism, inhibitors