Short communication

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

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\textbf{Abstract:}
Digoxin, a drug of narrow therapeutic index, is a substrate for common transmembrane transporter, P-glycoprotein, encoded by \textit{ABCB1} (\textit{MDR1}) gene. It has been suggested that \textit{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 \textit{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 \textit{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\textsubscript{min,s}) 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 ± 0.504 and 0.908 ± 0.358 for methyldigoxin (p < 0.02), respectively. No influence of \textit{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 \textit{ABCB1} genetic polymorphism, those modest changes are probably clinically irrelevant, and digoxin dose adjustment should include P-gp inhibitor co-administration rather than \textit{ABCB1} genotyping.

\textbf{Key words:}
\textit{ABCB1} polymorphism, P-glycoprotein, digoxin, genetic polymorphism, inhibitors