Comparison of DOS and Windows version of the MwPharm – a pharmacokinetic software for PK/PD monitoring of digoxin

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Background and objectives: Digoxin is the oldest drug indicated for the treatment of systolic heart failure (HF). It is also useful in controlling excessive ventricular rate in the presence of atrial arrhythmias. Therapeutic drug monitoring (TDM) has become an integral part of its prescription, allowing to optimize therapy and to reduce the incidence of toxicity. Since 1991, the MwPharm software package (Mediware, Groningen, The Netherlands / Prague, Czech Republic) has been used for pharmacokinetic and pharmacodynamic (PK/PD) modelling in TDM, including digoxin. First Windows version with a broader spectrum was released in 2014, as a reaction of worse support of the DOS background on later versions of Windows. After its release, the company had decided to not develop DOS versions anymore, even though they are globally used with success. The aim of this study was to compare the usefulness of DOS and Windows version (WIN) of the MwPharm, and their prediction quality in TDM of digoxin.
Materials and methods: 29 patients (23 with multidrug treated systolic HF, 4 with atrial fibrillation, 1 pregnant woman treated due to fetus tachycardia, 1 infant with Tetralogy of Fallot) who were treated for > 1 month with digoxin were eligible for inclusion. Patients received digoxin (Digoxin Léčiva®, Zentiva, Prague, Czech Republic) in a median dose 0.125 mg (range 0.063–0.250 mg) once daily. The therapeutic range for digoxin was established at 0.5–2.0 µg/l, according to manufacturer requirements. Both MwPharm versions (DOS version – MwPharm 3.30, Windows version – MwPharm++ 1.3.5) were used to parameterize the population PK model. Serum digoxin concentrations (SDC) were repeatedly examined and the differences between measured and calculated values predicted by both versions, including the percentage prediction error (%PE), were compared.
Results: SDC were obtained from 29 patients (mean age 67±20 years, body weight 72±27 kg). WIN, compared to DOS, used lower constants for absorption rate constant (ka) (0.61 vs 2.5), absolute bioavailability (F) (0.65 vs 0.7), total plasma clearance (CL) (6.11 vs 6.45 L/h), and extrarenal fraction (fe) (0.771 vs 0.783). Individual parameters calculated by WIN were consequently also lower – volume of distribution (V) (317 vs 354 l), renal fraction (fr) (0.62 vs 0.88), extrarenal fraction (fe) (0.55 vs 0.63), and elimination half-life ($t_{1/2}$) (59.4 vs 62.7 h). All values predicted by WIN were slightly lower but not significant. There was a close correlation between predicted and measured concentrations (Pearson's correlation coefficient: 0.008 vs 0.314, both $P < 0.0001$), and between SDCs predicted by both models (0.013, $P < 0.0001$). Their %PE was comparable (-0.43), too.
Conclusions: Actually used Windows version of the MwPharm software can be used for TDM interchangeably with popular, long-term used, but in these times unsupported DOS version.

Key words: MwPharm, therapeutic drug monitoring, digoxin, software.

Porovnání DOS a Windows verze MwPharm – farmakokinetického softvéru pro PK/PD monitoring digoxinu

Úvod a cíl práce: Digoxin je nejstarší lék užívaný v léčbě systolického srdečního selhání. Je rovněž účinný v kontrole nadměrného komorového rytmu v přítomnosti předsíňových arytmií. Terapeutické monitorování hladin léčiv (TDM) se stalo integrální součástí jeho preskripce, umožňující optimalizovat terapii a redukovat incidenci toxicity. Od roku 1991 se MwPharm (Mediware,

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