Effect of oseltamivir treatment on anticoagulation: a cross-over study in warfarinized patients

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

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WHAT THIS STUDY ADDS

In individuals taking warfarin at stable dosages for chronic vascular or cardiac conditions, there is no evidence for a pharmacodynamic or pharmacokinetic interaction between oseltamivir and warfarin that could alter the anticoagulant effect of the latter.

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AIM

To investigate whether oseltamivir enhances the anticoagulant effect of warfarin and to evaluate any pharmacokinetic (PK) interaction between the agents.

METHODS

Twenty volunteers (mean age 62 years) receiving daily warfarin and with INR values of 2.0–3.5 during the previous 2 weeks were randomized to concomitant oseltamivir 75 mg twice daily for 4.5 days or warfarin alone in a two-way cross-over design with a 4–8 day wash-out. Anticoagulant effects were assessed by calculating overall (AUEC(0,96 h)) and observed maximum effect (Emax) increase from baseline in INR, decrease from baseline in factor VIIa, and change in vitamin K1 concentrations. Plasma pharmacokinetics of (R)- and (S)-warfarin and oseltamivir were also assessed.

RESULTS

For both treatments, changes in INR and factor VIIa during treatment were small; for net AUEC(0,96 h), least square mean values were −9.53 (oseltamivir + warfarin) and −1.69 h (warfarin alone) for INR (difference −7.84 h, 90% CI −18.86, 3.17 h), and 1.56 and 0.54 kIU l−1 h, respectively, for factor VIIa (difference, 1.01 kIU l−1 h; 90% CI −1.18, 3.21). Differences between the treatments in Emax increase from baseline for INR, decrease from baseline for factor VIIa and change in vitamin K1 concentration were not statistically significant. Oseltamivir did not alter warfarin pharmacokinetics. Oseltamivir was well tolerated in this study with no clinically significant adverse safety findings.

CONCLUSION

Concomitant administration of oseltamivir for 4.5 days to volunteers on daily warfarin had little or no effect on warfarin pharmacokinetics and no effect on pharmacodynamics.