Oseltamivir lacks proarrhythmic potential leading to the onset of torsades de pointes

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Oseltamivir has been used for the treatment as well as prevention of influenza viral infection. Since sudden death after its administration has been reported, in this study we assessed the proarrhythmic potential of oseltamivir in comparison with a typical Ik channel blocker d-sotalol hydrochloride using the chronic atrioventricular conduction block (AVB) canine model. Moreover, in order to quantitatively assess their proarrhythmic potential, we used new marker of temporal dispersion of repolarization; namely, beat-to-beat variability of repolarization, which was calculated using 51 consecutive beats. Oseltamivir (3, 10 and 30 mg/kg/10 min, i.v., n=4) or d-sotalol hydrochloride (3 and 30 mg/kg, p.o., n=4) was administered to the AVB dogs with Holter ECG monitoring. Oseltamivir in any dose did not increase the beat-to-beat variability of repolarization or induced torsades de pointes, whereas its middle and high doses slightly prolonged the QT interval. On the other hand, d-sotalol prolonged the QT interval in both doses, increased beat-to-beat variability of repolarization in the high dose, and induced torsades de pointes in 1 out of 4 dogs in the low dose and in all animals in the high dose. These results indicated that intravenous administration of oseltamivir of up to 10 times of clinically recommended daily oral dose lacks proarrhythmic potential leading to the onset of torsades de pointes.

Keywords: oseltamivir, torsardes de pointes, QT prolongation