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Characterization of anti-atrial fibrillatory effect of anti-influenza drug oseltamivir assessed by the persistent atrial fibrillation dog, halothane-anesthetized dog and patch-clamp study

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Introduction: Anti-influenza drug oseltamivir delayed the atrial conduction and prolonged the atrial effective refractory period (AERP) in guinea pig hearts, and reduced the inducibility of burst pacing-induced atrial fibrillation (Af) in Langendorff-perfused rabbit hearts.

Methods: The canine persistent Af model (n=6) was prepared for the further in vivo characterization of the antiarrhythmic effect of oseltamivir. Moreover, we evaluated electropharmacological effect of oseltamivir on atria using the halothane-anesthetized dog (n=4). These results were compared with those of pure Na^+ channel blocker pilsicainide (n=6 and n=4, respectively). Furthermore, we evaluated the action of oseltamivir on ion channels expressed in HEK293 and CHO cells using the whole-cell patch-clamp technique (n=3).

Results: Oseltamivir (3 and 30 mg/kg) terminated the Af in 1 and 5 out of 6 animals, respectively, whereas pilsicainide (3 mg/kg) did it in 2 out of 6. Oseltamivir (0.3, 3 and 30 mg/kg) and pilsicainide (1 and 3 mg/kg) delayed the inter-atrial conduction in a dose- and frequency-dependent manner. Oseltamivir prolonged the AERP in a dose-dependent but frequency-independent manner, whereas pilsicainide did it in a dose- and frequency-dependent manner. IC_{50} values of oseltamivir against $I_{K,ACh}$, I_{Kr}, I_{Na}, I_{CaL} and I_{Kur} were 179, 225, >1000, >1000 and >1000 μM, respectively.

Conclusion: Oseltamivir can exert potent anti-Af effect through multi-channel inhibitory action, of which electrophysiological profile may be different from that of pilsicainide.