Utility of isoflurane-anesthetized guinea pigs for the assessment of the QT-interval prolongation induced by drugs with positive chronotropic action

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[Background] The QT interval can be shortened by tachycardia, which may underestimate risks of the drug-induced QT-interval prolongation in the safety pharmacology studies. To investigate utility of guinea pigs for the assessment of the QT-interval prolongation, we assessed cardiac effects of suspect drugs prolonging QT interval, sulpiride and aripiprazole, both of which exerted positive chronotropic actions in dogs.

[Methods] Under isoflurane-anesthesia, electrocardiogram and monophasic action potential (MAP) of right ventricle were continuously recorded from guinea pigs to measure the heart rate (HR) and the MAP duration (MAP_{90}), respectively. Sulpiride (2, 20, and 60 mg/kg) or aripiprazole (0.03, 0.3, and 3 mg/kg) were administered intravenously over 10 min.

[Results] Sulpiride at 2 mg/kg did not affect HR or MAP_{90}, and increased MAP_{90} with decrement of HR at 20 and 60 mg/kg. Aripiprazole at 0.03 and 0.3 mg/kg did not affect HR or MAP_{90}, and increased MAP_{90} with decrement of HR at 3 mg/kg. Meanwhile, positive chronotropic actions of sulpiride and aripiprazole were not observed.

[Conclusions] Since sulpiride and aripiprazole have been clinically reported to hardly induce tachycardia, anesthetized guinea pigs are useful for screening of drug-induced QT interval prolongation for safety pharmacology studies.