N-(3,4-DIMETHOXYCINNAMOYL) ANTHRANILIC ACID PREVENTS CANINE ATRIAL FIBRILLATION ASSOCIATED WITH TACHYCARDIA-INDUCED CARDIOMYOPATHY

ACC Poster Contributions
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Background: Inflammatory process is considered to be important for the pathogenesis of atrial fibrillation (AF). N-(3,4-dimethoxycinnamoyl) anthranilic acid, tranilast, is an antiallergic agent which has anti-inflammatory effects, but the effects on AF have not been elucidated. Thus, we assessed effects of tranilast on canine AF associated with tachycardia-induced cardiomyopathy.

Methods: Twenty beagles were allocated to Tranilast-treated dogs (N=7), no-drug control dogs (CTL, N=7) and sham operated dogs (N=6). Tranilast-treated dogs and CTL were subjected to atrial tachypacing (ATP, 400 bpm) without atroventricular block for 4 weeks. Tranilast was administrated orally (50 mg/kg/day) for 1 week before starting ATP, and continued throughout the protocol. The dynamics of atrial-tachycardia remodeling were evaluated by serial electrophysiological studies, and quantitative analysis of atrial fibrosis was performed.

Results: In CTL dogs, 4 weeks of ATP increased the duration of AF (from 0.3±0.2 to 40±6 sec, P<0.01), and decreased atrial effective refractory period (ERP; from 161±7 to 95±6 ms at basic cycle length 300 ms, P<0.01). Tranilast therapy attenuated ATP effects on the duration of AF (3.0±0.4 sec, P<0.01), without affecting ERP (106±4 ms, NS). ATP impaired hemodynamic parameters in CTL dogs (left ventricular ejection fraction: from 58±5 to 24±2%, P<0.01, left atrial area: from 311±17 to 456±39 mm², P<0.01), and increased atrial fibrosis (CTL 10.2±2.8 vs. Sham 0.6±0.1%, P<0.01). Tranilast suppressed ATP-induced atrial fibrosis (1.7±0.6%, P<0.01) without affecting left ventricular ejection fraction (29±3%, NS) and left atrial area (394±19 mm², NS).

Conclusions: Tranilast suppresses AF perpetuation in a canine model of AF by preventing atrial structural remodeling. Anti-inflammatory effects of tranilast may play an important role in the prevention of atrial structural remodeling.