ANTITHROMBOTIC EFFECTS OF DRONEDARONE IN AN IN VITRO STUDY

Poster Contributions
Poster Sessions, Expo North
Sunday, March 10, 2013, 3:45 p.m.-4:30 p.m.

Session Title: Arrhythmias: Atrial Physiology and Ablation of Atrial Arrhythmias
Abstract Category: 6. Arrhythmias: Other
Presentation Number: 1238-52

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Background: Results: from the ATHENA and PALLAS Trials showed that dronedarone impacts the rate of stroke in patients with atrial fibrillation. These unexpected findings cannot be explained solely by its antiarrhythmic effect and could involve an alternate mechanism of action. We investigated the possibility of dronedarone having a direct effect on blood thrombogenicity.

Methods: Blood samples collected from CAD patients (n=30) not taking antiplatelet (except aspirin) or anticoagulant medications were incubated with dronedarone's active metabolite SR35021A at 66 ng/ml (AM-1) and 119 ng/ml (AM-2), corresponding to the minimum and maximum mean Cmax reported after repeated 400 mg BID dosing. Control sample was incubated with equal volume of vehicle. Antithrombotic effects of dronedarone were assessed using coagulation time in ThromboElastoGraphy and whole blood platelet aggregation to ADP, collagen and TRAP.

Results: Coagulation Time was significantly longer in samples incubated with AM-1 and AM-2 compared to control (mean ± SD of 180 ± 22 and 182 ± 32 seconds vs. 164 ± 25 seconds, respectively p<0.01). Platelet aggregation was lower in AM samples than in control, but achieved statistical significance only in AM-2 samples in response to ADP and TRAP (p<0.05) [see Figure].

Conclusions: Dronedarone demonstrates direct anti-coagulant and anti-platelet properties. In vivo clinical studies are needed to confirm these findings.