Poster Session II

PO-641-07

PATIENTS WITH LONG QT SYNDROME HAVE A PRIMARY SINOATRIAL NODE PHENOTYPE OF INTRINSIC CHRONOTROPIC INSUFFICIENCY
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Background: Long QT syndrome (LQTS) is a cardiac channelopathy characterized by QT prolongation and the potential for ventricular torsadogenic-mediated syncope, sudden cardiac arrest, and sudden cardiac death. Whether patients with LQTS have a primary sinoatrial node (SAN) phenotype of chronotropic insufficiency has been speculated but not demonstrated because of the confounding effects of beta blocker therapy.

Objective: To determine whether there is intrinsic chronotropic insufficiency present in untreated patients with LQTS.

Methods: A retrospective review of all treadmill exercise stress tests (TEST) was performed on patients with one of the three most common LQTS genotypes: LQT1, LQT2, and LQT3. For each patient, the first TEST completed while off beta blocker was analyzed. Patients with prior cardiac sympathetic denervation therapy were excluded. Chronotropic insufficiency was defined as having an age- and gender-predicted peak heart rate (HR) < 85% and/or a predicted HR reserve < 80%.

Results: Overall, 339 LQTS patients (197 LQT1, 73 LQT2, and 69 LQT3) were included (189 female [56%]; mean age at time of TEST [28 ± 17 years]). Mean predicted peak HR for all LQTS patients was 88% (range 54% - 119%) and mean predicted HR reserve was 79% (range 19% - 134%). Overall, half of all LQTS patients (n = 177; 52%) displayed chronotropic insufficiency, of which 129 with LQT1 (65%), 30 with LQT2 (41%), and 18 with LQT3 (26%). Patients with LQT1 were most likely to exhibit chronotropic insufficiency compared to patients with LQT2 (p = 0.0006) and LQT3 (p = 0.0003). There was no difference between patients with LQT2 and LQT3 (p = 0.06). Presence of chronotropic insufficiency was not a predictor of LQTS-associated symptoms.

Conclusion: Patients with LQTS, particularly LQT1, have an SAN phenotype of chronotropic insufficiency. If assessing beta blocker therapy effect by impact on peak HR, the patient’s pre-treatment peak HR, rather than an age- and gender- predicted maximum HR, should be used.

PO-641-08

VERY LOW EFFICACY OF VAGAL MANEUVERS IN TERMINATING PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA: RESULTS FROM THE NODE-301 STUDY
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Background: Vagal maneuvers (VMs) are often recommended to individuals with paroxysmal supraventricular tachycardia (PSVT) approved for self-administration outside a medically supervised setting. VMs are associated with non-dihydropyridine, L-type calcium channel blocker in development to treat atrioventricular nodal-dependent PSVT. NODE-301 (NCT03464019) was a randomized, placebo-controlled, multicenter, phase 3 study evaluating self-administration of 70 mg etripamil nasal spray for acute termination of PSVT episodes in patients aged ≥ 18 years.

Objective: To determine the effectiveness of VMs as a first-line treatment in resolving PSVT episodes prior to study drug treatment in the NODE-301 study.

Methods: Patients were trained on VMs and instructed by study physicians to use a VM as their first attempt to resolve a perceived SVT episode within a 5-hour monitoring period. If the VM was unsuccessful in terminating the episode, patients self-administered study drug (etripamil or placebo). Exploratory efficacy endpoints included the number of SVT episodes (as assessed by an independent adjudication committee) that were successfully terminated (converted to sinus rhythm as assessed by ECG) by a VM alone and were described via descriptive statistics.

Results: Overall, 208 of 431 (48.3%) patients perceived an episode of PSVT. In total, VMs were performed on 171 (97.7%) of 175 confirmed (positively adjudicated) PSVT episodes. VMs by themselves terminated 10 of 171 (5.8%) confirmed PSVT episodes. For the remaining symptomatic PSVT episodes that persisted after VMs, 156 were treated with study drug. The Kaplan-Meier estimate showed that 54% of etripamil- and 35% of placebo-treated episodes terminated within 30 minutes.

Conclusion: In this study, VMs alone were rarely successful in terminating symptomatic sustained PSVT episodes. Patients with recurrent PSVT episodes should be counseled regarding the limited efficacy of VMs. There remains an unmet therapeutic need for a safe and effective at-home therapy to reliably terminate PSVT.