B-TYPE NATRIURETIC PEPTIDE MAY PROMOTE ARRHYTHMIA IN HEART FAILURE THROUGH INHIBITING TRANSIENT OUTWARD POTASSIUM CURRENT

Poster Contributions
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Background: Elevated B-type natriuretic peptide (BNP) levels were shown to independently predict both the occurrence of sudden cardiac death and ventricular arrhythmia in heart failure (HF) in addition to left ventricular ejection fraction and HF class. Previous studies reported that intravenous BNP (iv-BNP) could improve HF symptoms but was linked with increased risk of death in HF patients. Our study aimed to test whether iv-BNP directly contributes to proarrhythmic effect.

Methods and Results: A total of 1878 patients (pt) admitted for class III/IV HF from 01/2004 to 12/2009 were reviewed with 1084 pts received iv-BNP (2μg/kg iv bolus followed by 0.01μg/kg/min infusion). QTc interval on12-lead surface ECG, measured in 61 pts without bradycardia or tachycardia, ventricular pacing and QT-prolonging drugs or electrolyte abnormalities, was slightly but significantly longer with iv-BNP administration (465.78±49.14 ms vs. 456.15±52.04 ms at baseline, p<0.01). Heart rate decreased from 84.10±18.96 beat-per-minute to 81.43±16.11 beat-per-minute (p=0.014). In 106 pts with complete telemetry data, the frequency of premature ventricular contraction (PVC) and/or nonsustained ventricular tachycardia (NSVT) was significantly increased during iv-BNP (p=0.019). Compared to a control group of 50 of 794 HF pts with comparable demographic characteristics but without iv-BNP infusion, pts during iv-BNP have significant increased incidence of PVC (p=0.0068) and NSVT (p=0.0324). To investigate the cellular electrophysiology mechanism, the effects of human BNP on major repolarizing currents were investigated in HEK-293 cell lines with stably expressed human KCNQ1/KCNE1 (slow delayed rectifier potassium current, IKs), KCNH2 (rapid delayed rectifier potassium current, IKr), and KCND3/KCNE2 (transient outward potassium current, Ito). The results showed that BNP over clinically relevant range (0.1~100nM) significantly inhibited Ito in a dose dependent manner with IC50 of 24.9±0.05nM but had no effects on IKs and IKr.

Conclusion: Our study suggests that BNP may contribute to the increased susceptibility to arrhythmogenesis in HF which may result from its direct inhibition of Ito.