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P578 Adenosine A2A receptor inhibition stabilizes the rate dependent beat-to-beat response of L-type calcium current in human atrial myocytes

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Purpose: Electro-mechanical alternans heralds the onset of several cardiac arrhythmias, and adenosine A2A receptor (A2AR) stimulation favour the occurrence of beat-to-beat alternations in the L-type calcium current (ICa) at high stimulation frequencies. The purpose of this study was to test whether A2AR inhibiton is able to increase the threshold frequency for activation of ICa alternation in human atrial myocytes.
Methods: Isolated human atrial myocytes were subjected to patch-clamp technique in order to measure the L-type calcium current (ICa) activated by depolarization to 0 mV and the tail current (Itail) elicited upon repolarization. The stimulation frequency was increased stepwise from 0.2 to 2 Hz.
Results: In control conditions, uniform beat-to-beat patterns of both ICa and Itail were observed in all of 45 myocytes at low stimulation frequencies and throughout all stimulation frequencies in 8 of the 45 cells. In 26 of the 45 cells an alternating beat-to-beat pattern was observed at stimulation frequencies between 0.67 and 2 Hz. The alternating pattern was gradually replaced by an irregular pattern as the stimulation frequency was increased to 2 Hz, where an irregular pattern was observed in 35 of the 45 myocytes. When exposed to the selective A2AR antagonist ZM241385 (50 nM), a uniform pattern was maintained in a larger fraction of cells at higher stimulation frequencies. This was reflected in a shift in the frequency of appearance of non-uniform (alternating or irregular) beat-to-beat alternation from 1.5±0.2 Hz in control to 1.9±2 Hz with ZM241385 ($p=0.02$, n=17). A similar effect was seen when baseline activation of the A2AR was prevented by inclusion of adenosine deaminase (ADA, 2 units/ml) in the extracellular solution. Indeed, ADA shifted the frequency of appearance of non-uniform patterns from 1.3±0.1 Hz in control to 1.7±0.1 Hz ($p<0.001$, n=28). Infusion of 30μM adenosine, the natural A2AR ligand, through the patch pipette lowered the threshold for non-uniform patterns from 1.3±0.2 Hz in control to 0.6±0.2 Hz with adenosine. Subsequent inclusion of ZM241385 in the external solution reversed the effects of adenosine, increasing the threshold for non-uniform patterns from 0.6±0.2 to 1.4±0.2 Hz ($p<0.05$, n=4).
Conclusions: In human atrial myocytes, adenosine A2A receptor antagonism stabilizes the rate-dependent beat-to-beat response of ICa both at baseline and at elevated cytosolic adenosine levels. This points to the importance of adenosine A2A receptors in the dynamic regulation of intracellular calcium.

P579 Propafenone and Flecainide increase the current through human cardiac Kir2.1 channels

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Purpose: Propafenone (P) and flecainide (F) are two class Ic antiarrhythmic drugs widely used in the treatment of cardiac arrhythmias. Unfortunately, both exhibited also ventricular proarrhythmic effects that limit their use. The inward rectifying K^+ current (IK1), mainly carried by Kir2.1 channels, is critical in determining the resting membrane potential (RMP) and shaping the initial depolarization and the final repolarization phases of the cardiac action potential (AP). Furthermore, it has been demonstrated the importance of the IK1 increase in the establishment of a fast and stable reentry of spiral electrical waves (rotors) and fibrillation dynamics. Thus, the effects of P and F on human cardiac Kir2.1 channels have been studied.
Methods: Kir2.1 currents (IKir2.1) were recorded in transiently transfected in Chinese hamster ovary cells using the whole-cell configuration of the patch-clamp technique.
Results: F (0.5-20 μM) produced a concentration-dependent increase in IKir2.1, the effect being more marked at potentials positive than negative to the K^+ reversal potential (EK). Indeed, F (1 μM) increased ($P<0.05$) the IKir2.1 by 46.6±11% and 16.4±2.6% at -50 and -120 mV, respectively (n=6). The effects were apparent at extracellular K^+ concentrations of both 4 and 140 mM, but only blockade was observed when F was applied to the intracellular surface of the membrane in inside-out patches. When using an AP voltage clamp protocol, F increased the total charge flowing through Kir2.1 channels during the AP by 135±22% (n=6, $P<0.01$). P (0.5-50 μM) produced a concentration-dependent inhibition of IKir2.1 (IC50=4.7±0.6 μM) at potentials negative to the EK but increased the current at potentials positive to the EK (50.8±9.4% increase produced by 1 μM P at -50 mV, n=5). P (1 μM) increased the total charge flowing through Kir2.1 channels during the AP by 131±39% (n=7, $P<0.01$).
Conclusions: the results demonstrated that both P and F at therapeutically relevant concentrations increased the current through Kir2.1 channels an effect that could affect their Na^+ blocking properties by hyperpolarizing the RMP and contribute to their proarrhythmic effects.

CARDIAC REHABILITATION

P580 The Italian SurveY on carDiac rEhabilitation (ISYDE-2008). Patients characteristics and current provision of cardiac rehabilitation

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Background: comprehensive cardiac rehabilitation (CR) and secondary prevention are recognized as effective approach for cardiovascular risk reduction and long-term care of cardiac pts.
Aim: to provide specific information on characteristics of pts admitted to CR, diagnostic procedures, exercise and educational programs, treatment, and to compare current provision with National GL.
Methods: the ISYDE-2008 is a multicenter, longitudinal, prospective national registry, designed by the Italian Association for Cardiovascular Prevention Rehabilitation and Epidemiology to collect data on organization and core components of CR in Italy. The study population consisted of 2281 consecutive pts, discharged from 165 Italian CR centres from Jan 28th to Feb 10th 2008.
Results: age was 67±10.5 yrs (26.5% women). Indications for CR were: CABG in 30.1%, valvular surgery 15.8%, combined 7.5%, thoracic surgery 2.4%, ACS 8.8%, PTCA 14.2%, heart failure 12.5%, CPD 1%, angina 1.8%, other 5.8%. 67.0% of pts had ≥1 comorbidity: prior AMI 22.1%, PTCA 9.9%, cardiac surgery 11.0%, carotid atherosclerosis 7.0%, CPD 6.6%, abdominal aortic aneurism 1.8%, respiratory insufficiency 4.9%,renal failure 8.8%, hepatic disease 2.8%, neurological disease 6.4%, diabetes 20.8%, orthopedic disease 9.1%. 1159 pts (50.8%) had 3-5 CVD risk factors and 9.3% >5.
38.5% of pts had ≥1 complication during CR: 8.9% atrial fibrillation, 1.9% arrhythmias, 0.6% PM, 0.4% AMI, 0.7% stroke/TIA, 1.9% minor and 6.6% peripheral neurological damage, 7.1% anemia, 3.1 acute renal failure or 0.3% liver failure, 0.4% surgical wound revision, 1.4% thoracentesis, 0.1% pericardial drainage, 0.1% PNX, 0.1% redo surgery, 1.0% inotropic infusion, 1.0% mechanical ventilation, 0.04% pulmonary embolism, 2.9% infection, 1.4 transfusion, 15.7% other.
During CR 43.1% pts had a 6-min walk test at admission and 41.5% at discharge, 19.6% and 30.9% an exercise test, 5.3% and 6.9% a cardiopulmonary test; 0.5% electrical and 1.4% pharmacological cardioversion, 88% cardiacecho (LVEF >50% in 59%) and 16% vascular ultrasound.
At discharge, 72% pts received ACEi/ARBs, 68% b-blockers, 51% diuretics, 66% statins, 16% n-3PUFA, 26% oral anticoagulant, 66% ASA, 24% other antiplatelet agents, 2.4% LW Heparin, 19% nitrates, 5.4% digitalis, 19% CCBs, 9% insulin, 15.5%antidiabetics, 5.8% amiodarone, 6.2% anti-depressive. A long term prevention program was scheduled for 54% pts.
Conclusion: surveys and registries are effective means of assessing the implementation of GL. The ISYDE-2008 broad participation offers a detailed snapshot of current CR provision, organization and activities

P581 Comparison of hospital-based versus home-based exercise training in patients with heart failure: effects on functional capacity, quality of life, psychological symptoms, and hemodynamic parameters

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Objective: Heart failure (HF) is a common and disabling syndrome that is the final common pathway for a number of cardiac conditions. Despite major advances in the pharmacological treatment of HF, the number of patients afflicted with HF is rising yearly, and a large number of patients suffer from dyspnea, fatigue, diminished exercise capacity, and poor quality of life It has been suggested that exercise training is a crucial and effective method in the treatment of HF patients. In the majority of the studies that have been conducted in this area, either hospital or home-based exercise groups have been chosen as control groups, but no studies have compared the effects of these two types of exercise groups. Therefore, our study aims to compare the effects of home-based and hospital-based exercise programs on exercise capacity, quality of life, psychological symptoms, and hemodynamic parameters in HF patients.
Methods: Seventy-four patients were divided into either a hospital-based exercise (group 1) or a home-based exercise (group 2) group. Before and after the 8 week rehabilitation program, the patients in the two groups were compared with respect to functional capacity [maximal oxygen uptake (pVO2), a six minute walk test (6MWT)], quality of life (Medical Outcomes Study, the 36-item Short Form Survey, SF-36), psychological symptoms [Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI)] and hemodynamic parameters [(left ventricular diastolic dysfunction (LVDD), left ventricular diameter in systole (LVDS), Mitral Early diastolic peak flow velocity (E)/late diastolic peak flow velocity (A), Mitral E/Mitral early peak velocity (Em), Tei index, right ventricule systolic peak velocity (Sm), Tricuspid annular plane systolic excursion (TAPSE), systolic pul-