1200-169 Effects of Chromanol 293B on Outward Currents and Action Potentials in Human Atrial Myocytes

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Background: The role of I_{Ca} in the human atrium is unclear. Therefore, the effect of Chromanol 293B (Chrom), a recently described highly selective I_{Ks} blocker in guinea pig ventricular myocytes, was investigated in human atrial myocytes.

Methods: Specimens of human atrial appendages were obtained from patients undergoing coronary bypass surgery. Patients had stable sinus rhythm and received no antiarrhythmic drugs. Freshly enzymatically isolated myocytes were studied by whole cell patch clamp techniques.

Results: Chrom (10 μM) prolonged action potential duration at 90% depolarization in cells of 8 patients with 16 ± 2.7 ms (mean ± SEM) at 1 Hz, with 15.4 ± 2.4 ms at 2 Hz and with 17.3 ± 2.5 ms at 3 Hz stimulation frequency. APD 50% remained unchanged in the presence of 10 μM Chrom. A small (60) current (inward 40 pA) was inappropriately observed at a potential of −40 mV after depolarizing pulses from −80 mV to −30 until +60 mV. 1 μM dofetilide was used to block I_{Ca}. Chrom blocked the dofetilide-insensitive tail current with 88 ± 7% after short depolarizing pulses (200 ms) to +60 mV and almost completely suppressed this I_{Ca} after long pulses (2000 ms). For the investigation of I_{Ks}, 2 mM CoCl₂ was used in order to suppress I_{Ca} and I_{KCl}. Chrom (10 μM) blocked peak I_{Ks} with 26 ± 3% at pulses to +70 mV, while the sustained outward current remained unchanged at this concentration. Using 3, 10, 50 and 100 μM Chrom, I_{Ca} for dofetilide blockade was calculated as 29 ± 5 μM. In summary, the effects of chrom on action potentials of human atrial myocytes can be due to blockade of I_{Ca} and I_{Ks}.

Conclusion: Although I_{Ca} is difficult to detect and small in amplitude, our data point out to a significant role of I_{Ca} in the repolarization of the human atrium, since the frequency-independent action potential prolongation in phase 3 is unlikely to be exclusively an I_{Ks} effect.

1200-170 Impaired Effect of Dofetilide on the Delayed Rectifier Potassium Current During Acidois

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Background: Acidosis is an important factor in the setting of myocardial ischemia. In the present work, we investigated the effect of the new class III antiarrhythmic agent dofetilide on the delayed rectifier K⁺ current (I_{Ks}) under different extracellular H⁺ concentrations.

Methods: Isolated guinea pig cardiomyocytes were used for the whole cell patch-clamp experiments. Depolarizing pulses of 200 ms were applied to different cell patches, and tail currents at 20 ms after depolarization were measured. The initial tail currents were measured at −100 mV, and then the membrane potential was returned to the holding potential, and the tail currents were measured at −70 mV for 1000 ms.

Results: At physiological pH, dofetilide decreased both the time-dependent current and the tail currents in a dose-dependent manner at concentrations >10 μM. However, at an extracellular pH of 6.8, time-dependent currents were only significantly decreased at concentrations >10 μM (−34 ± 4% for 10 μM at +90 mV, p < 0.05). Tail currents were already significantly decreased by the administration of 10 μM dofetilide, though only by −20 ± 6% (pH = 6.8) compared to −51 ± 3% at a pH of 7.4 (p < 0.05).

Conclusions: Inhibition of I_{Ks} by dofetilide was decreased during acidosis. Since increasing the extracellular H⁺ concentration should increase the protonated form of dofetilide, it is suggested that the protonized form of dofetilide is the one responsible for its class III drug action. This may imply a loss of antiarrhythmic efficacy of dofetilide during acidosis.

1200-171 A Novel Inwardly-Rectifying Transient Outward Potassium Current Plays an Important Role in Maintaining Cell Excitability of Canine Myocardium

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Background: We have previously described a novel inwardly-rectifying transient outward K⁺ current (I_{K1}) in canine ventricular myocytes. I_{K1} is sensitive to the application of Ba²⁺, and activates upon depolarization over a time course comparable to I_{Ca} pointing to possible action of it in cell excitability.

The present study determined the role of I_{K1} in maintaining cardiac excitability.

Methods: We used whole-cell patch configuration (36°C) to record action potentials (APs) and current. Cell excitability was determined with variable rectangular current steps by measuring minimum current intensity for triggering APs, and the intensity-duration curve was plotted in the absence and presence of Ba²⁺.

Results: The intensity-duration curve was substantially shifted to left-down direction by the addition of Ba²⁺ (1 and 5 μM), indicating an increase in cell excitability. The minimum current intensity (3 ms duration) for triggering APs was decreased from 142 ± 21 pA (control) to 116 ± 19 and 82 ± 18 pA (P < 0.01, n = 8) in the presence of 1 and 5 μM Ba²⁺. At voltage step (300 ms) to −20 mV from a holding potential of −80 mV, I_{K1} was 1.8 ± 0.5 nA in control, and reduced respectively to 1.3 ± 0.1 and 0.9 ± 0.2 nA after the addition of 1 and 5 μM Ba²⁺ (P < 0.01, n = 7).

Conclusion: Ba²⁺-induced increase in cell excitability in corresponding to the reduction of I_{K1}, and therefore, I_{K1} plays an important role in maintaining cardiac excitability, particularly in increased [K⁺], as in acute myocardial ischemia.
All numbers in mm, and in mean ± SD. TA, TT, base, lengths of incised annulus (TA), incision of coronary sinus (CSO), diameter of right & distal CSO, AVN, AVN-CSO, distance between AV nodal artery ending and bundle (H) site of CSO roof. Compared to group B, group A had a longer CSO axe with a stiffer tapering of the CSO lumen and a more low-setting of the AV node, but had similar dimensions of the Koch's triangle.

Conclusions: Pts with clinical AVNRT had a lower AV node position within the Koch's triangle and a closer proximity to a larger CSO, which may create an electrophysiological milieu for the development of AVNRT.

1201-162 Fluoroscopic Dimensions of the Triangles of Koch and Feasibility of Radiofrequency Ablation of the Slow Nodal Pathway


The dimensions of the triangle of Koch (TK) may influence the ease for slow nodal pathway (SP) ablation. In 65 consecutive patients (Pts) (45 ± 10 years, 71% female) submitted to radiofrequency catheter ablation (RFCA) of the SP, manual injection of contrast into the right atrium was used to visualize the septal leaflet of the tricuspid valve (TVS). Angiographic references in RAO projection were: a) tip of the His catheter (Hc); b) point of injection of the catheter entering the coronary sinus (CSOs) c) anterior limit of the TVS; d) anterior limit of the TVS. Reference for measurements: electrodes of the Hc. Dimensions obtained (Figure): 1) Hc-CSOs (fluoroscopic Todor 2) horizontal distance from the mid point of the FT to the anterior limit of the TVS (med Koch); 3) horizontal distance from the CSOs to the anterior limit of the TVS (TK base); 4) vertical distance from the CSOs to the inferior limit of the TVS [Eustachian-tricuspidal peak (ETP)]. RF applications (app) for ablation 4 ± 4.6 (median 2). Pts were divided into two groups: A: <2 app (38), B: >2 app (27). There were no differences in age or sex. An ETP was more frequent in group B than in group A (38% vs 59% p < 0.01).

Conclusions: RFCA of the SP may be more difficult, requiring a greater number of RF applications, in Pts with a wide TK base, and specially in those with a well developed ETP.

1201-163 Effect of Radiofrequency Catheter Ablation of Accessory Pathways on Autonomic Tone in Children

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Background: Radiofrequency catheter ablation (RFCA) of supraventricular tachycardia (SVT) is increasingly being used as a curative approach in the pediatric population. Inadequate effects of RFCA on cardiac autonomic function have been described in adults, but have never been evaluated in children.

Methods: We determined the effects of RFCA on invasive and noninvasive parameters of cardiac autonomic function in eight children (5-16 y.o., 6 male, 2 female) with inducible AV reciprocating tachycardia (AVRT) before and within 24 hours after successful RFCA of accessory pathways (7/8 concealed; 2 right, 6 left-sided).

Results: (mean ± standard deviation)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before RFCA</th>
<th>After RFCA</th>
<th>p</th>
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<tbody>
<tr>
<td>Sinus cycle length (SCL)</td>
<td>636 ± 157</td>
<td>679 ± 47</td>
<td>0.03</td>
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<tr>
<td>AH interval (at 100 m/s)</td>
<td>121 ± 13</td>
<td>94 ± 17</td>
<td>0.017</td>
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<tr>
<td>Atrial ERP (at 500 m/s)</td>
<td>238 ± 55</td>
<td>235 ± 36</td>
<td>NS</td>
</tr>
<tr>
<td>Wenkebach cycle length (WCL)</td>
<td>370 ± 39</td>
<td>285 ± 24</td>
<td>0.02</td>
</tr>
<tr>
<td>Wenkebach ERP (at 500 m/s)</td>
<td>235 ± 14</td>
<td>223 ± 16</td>
<td>0.043</td>
</tr>
<tr>
<td>Baroreceptor sensitivity</td>
<td>3.83 ± 1.7</td>
<td>4.52 ± 2.88</td>
<td>NS</td>
</tr>
<tr>
<td>Valsalva (RR ratio)</td>
<td>1.66 ± 0.38</td>
<td>1.61 ± 0.17</td>
<td>NS</td>
</tr>
<tr>
<td>Deep breathing (respiratory change)</td>
<td>57 ± 23</td>
<td>45 ± 29</td>
<td>NS</td>
</tr>
<tr>
<td>Response to tilt (change in heart rate at 2 min)</td>
<td>20 ± 18</td>
<td>26 ± 11</td>
<td>NS</td>
</tr>
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</table>

Standard time- and frequency domain parameters of 24 hour heart rate variability analysis did not change significantly following RFCA. The changes in SCL, WCL and ERPs were abolished by pharmacologic autonomic blockade with atropine and esmolol.

Conclusion: In pediatric patients, RFCA of accessory pathways is associated with changes in electrophysiologic parameters consistent with increased sympathetic and/or decreased parasympathetic tone.

1201-164 Intravenous Dobutamine for Termination of Paroxysmal Supraventricular Tachycardia

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Abstract: Dobutamine (DOP), a new, highly selective potassium channel blocker, was tested for acute termination of sustained re-entrant paroxysmal supraventricular tachycardia (PSVT).

In a multicenter, double blind trial, 86 patients were randomized equally to either placebo (PLA) or IV infusion of DOP at 8 mg/kg for 15 mins. The patient population included 51 males and 45 females between ages 18 and 85. PSVT occurred spontaneously in 6 patients and was induced in the lab in 90.

DOP and PLA groups were matched for age, gender, structural heart disease, and mechanism of PSVT. Patients were observed for 30 mins. after the start of infusion. The rate of conversion and the time to conversion were compared: 36 of 48 patients (81%) in the DOP group converted to sinus rhythm, vs 18 of 48 patients (38%) in the PLA group (p < 0.001). The time to conversion was also significantly shorter (median = 9.5 mins) for DOP vs PLA (p = 0.0001).

There were no serious adverse events and no proarrhythmias. The incidence of treatment emergent adverse events of all causalties was slightly smaller on DOP (25%) than on PLA (31%).

Conclusion: IV DOP was more efficacious than PLA in terminating PSVT. It was well tolerated and no proarrhythmic events were observed.

1201-165 Efficacy and Safety of Intravenous Dobutamine in Acute Conversion of Supraventricular Arrhythmias in Wolff-Parkinson White Syndrome

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Background: Intravenous dobutamine is a class III antiarrhythmic agent and selective potassium channel blocker for LR, which may be useful in the acute management of supraventricular tachycardia.

Methods: Fifteen male patients (age 34 ± 13 yrs, range 18-63 yrs) with preexcitation on ECG underwent electrophysiologic (EP) testing and induction of sustained AV reentrant tachycardia (n = 4) or atrial fibrillation (n = 12). Patients were randomized to receive an infusion of either placebo (n = 5), dobutamine 2.5 mcg/min (n = 5), or dobutamine 4 mcg/min (n = 5) over 15 minutes. Non-responders received a second infusion of higher dose dobutamine (2.5-6 mcg/min) for 15 minutes and underwent repeat EP testing.

Results: Two of five patients responded to 2.5 mcg/min dobutamine and 4/5 patients responded to 4.0 mcg/min dobutamine, compared to 1/5 patients with placebo. After a second infusion of higher dose dobutamine (including placebo crossover), 11/15 patients responded to dobutamine (73%). One patient experienced mild pain at the infusion site. There were no study discontinuations, proarrhythmias or serious adverse events.

Conclusion: Intravenous dobutamine is a safe and promising agent for acute termination of supraventricular arrhythmias in the Wolff-Parkinson White Syndrome.

1202 Ventricular Arrhythmias: Mechanism and Ablation

Wednesday, April 1, 1998, Noon-2:00 p.m. Georgia World Congress Center, West Exhibit Hall Level Presentation Hour: Noon-1:00 p.m.

1202-173 Sympathetic Potential During Ventricular Tachycardia Are Indicative of Critical Sites Within the Reentry Circuit in Patients With Coronary Artery Disease

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Background: Isolated diastolic potentials (IDP) have been found to be helpful in locating critical sites within the reentry circuit in patients (pts) with ventricular tachycardia (VT) and coronary artery disease (CAD). Isolated potentials