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Effects of beta-adrenoceptor stimulation on human atrial voltage-dependent K+ currents

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Purpose: The electrophysiological effects of β-adrenergic stimulation on atrial myocytes obtained from patients in sinus rhythm (SR) and chronic atrial fibrillation (CAF) have not been compared until yet, even when it has been proposed that β-adrenergic stimulation has profound influence in the genesis and maintenance of atrial fibrillation. Therefore, we analyzed the effects produced by isoproterenol (Iso, 1 nM), a β-adrenoceptor agonist, on the transient outward (Ito), the ultrarapid (IKur) and the slow delayed rectifier (IKs) K^+ currents recorded in human atrial myocytes obtained from SR and CAF patients.

Methods: Currents were recorded in enzymatically dissociated myocytes obtained from right (RAA) and left (LAA) atrial appendages from SR and CAF patients using the patch-clamp technique.

Results: In SR myocytes Iso slightly inhibited the Ito (by 10.1±6.6% in RAA and 15.6±3.3% in LAA myocytes at +30 mV, P>0.05). In CAF myocytes, the Iso-induced Ito inhibition reached a 24.9±6.2% in RAA (P<0.05 vs SR) and was even significantly greater in LAA (36.5±4.9%) cells. In RAA and LAA myocytes from SR and CAF patients, Isus was not significantly modified. Moreover, in SR myocytes Iso did not modify the IKs (4.5±2.6% augmentation in RAA and 6.6±1.4% in LAA myocytes at +30 mV) which was almost undetectable (25.0±4.5 pA at +30 mV). Conversely, as we previously demonstrated IKs amplitude significantly increased in both RAA and LAA CAF myocytes (59.7±8.3 pA at +30 mV, P<0.01 vs SR), and, under these conditions β-adrenergic stimulation increased the IKs by 51.8±6.2% in RAA and by 78.0±12.4% in LAA myocytes (P<0.05 vs CAF RAA). Moreover, in both SR and CAF myocytes atenolol, a selective β1-adrenoceptor antagonist, abolished Iso effects on Ito and IKs. Furthermore, a real-time q-PCR analysis demonstrated that the β1-adrenoceptor mRNA expression was significantly higher in CAF than in SR samples and that this CAF-induced up regulation was significantly more marked in the LAA than in the RAA.

Conclusions: We concluded that CAF potentiates the β1-adrenergic effects on Ito and IKs an effect produced by means of an up-regulation of the β1-adrenoceptors which was greater in LAA than in RAA myocytes. The CAF-induced increase in the IKs amplitude and in the β1-adrenergic stimulating effects could contribute to the shortening in the duration of the atrial action potential and refractoriness observed in CAF.