An Investigation In The Effect Of Short Acting β-Adrenoceptor Agonist On Myocardial Injury In A Pre-Clinical Heart Attack Model.

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Short acting β-adrenoceptor agonists (SABA) are widely used to treat symptoms of chest tightness commonly associated with Asthma and Chronic Obstructive Pulmonary disease (COPD). Recent studies have associated increased in morbidity and mortality in respiratory patients with these conditions with underlying heart disease currently being treated with SABAs (Au et al., 2002; Cazzola et al., 2005)

The current study aimed to investigate the effects of SABA, Salbutamol on the myocardium subjected to ischaemia-reperfusion (I/R). Langendorff hearts were subjected to control or I/R in the absence or presence of Salbutamol (1-100nM) ± CGP-20712 (β₁ adrenoceptor selective antagonist, 1nM) or ICI-118551 (β₂ adrenoceptor selective antagonist, 1µM). Hearts underwent triphenyl tetrazolium staining for infarct size assessment. In separate experiments isolated rat cardiomyocytes were exposed to simulated I/R in the absence or presence of Salbutamol (1pM-1µM) ± CGP-20712 or ICI-118551. Cellular injury was determined by measurement of viable, apoptosis and necrosis using flow cytometry. Hypercontracture was also assessed in cardiomyocytes subjected to oxidative stress in the absence or presence of Salbutamol using confocal microscopy.

Salbutamol (100nM) significantly increased infarct size to risk ratio (%) compared to controls (76±3% vs. 51±2%, P<0.001, respectively, n=7-9). Administration of Salbutamol in the presence of the CGP-20712 or ICI-118551 blocked the cardio-toxic effects of Salbutamol to varying degrees (63±4%, P<0.01, 50±2%, P<0.001, respectively). Salbutamol significantly increased apoptosis/necrosis compared to non-treated cardiomyocytes subjected to hypoxia/reoxygenation, the cardio-toxic effect of Salbutamol was significantly abrogated by CGP-20712 and ICI-118551 (n=7-10). Salbutamol also significantly reduced hypercontracture time in cardiomyocytes subjected to oxidative stress (n=8).

This study is the first to identify the cardiotoxic effects of SABA, Salbutamol in a pre-clinical heart attack model. Further studies are currently being investigated to determine the mechanism of action of the cardiovascular events associated with certain SABAs such as Salbutamol.

References
