Measuring Physiological Response of Bisphenol-A on Cardiac Excitation-Contraction Coupling

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Introduction

Bisphenol-A (BPA) is an endocrine-disrupting compound (EDC) commonly found in consumer plastics. Environmental exposure varies between 1–100 nM, while clinical and industrial exposure can reach 10 μM. The aim of this project is to determine the effects of BPA on cardiac mechanical function and calcium handling.

Objectives

To detect the effects of BPA exposure (15 min) on left-ventricular developed pressure (LVdP) and contractility (dP/dt). To monitor changes in epicardial calcium handling with increasing BPA doses and pacing frequencies.

Methods

We aimed to test the direct effects of BPA on cardiac function using a Langendorff-perfusion model. Excised female rat hearts were treated with 1 nM-10 μM BPA and the resulting effects on cardiac mechanical function and calcium handling were monitored. For calcium imaging, excised hearts were treated with Blebbistatin to arrest mechanical function, and then stained with Rhod-2, a calcium indicator dye. Epicardial calcium transients were recorded using an Andor CCD camera equipped with wavelength specific filters (570±30 nm), and an LED spotlight (535 nm) was used for dye excitation. Calcium transients were initiated at various pacing frequencies (5Hz, 6.6Hz, and 9Hz). To assess the effect of BPA on the mechanical function of the heart, a latex balloon was inserted into the left-ventricle to quantitate left-ventricular developed pressure (LVdP) and maximum contractility.

Results

Previous studies have shown that BPA exposure can prolong ECG PR segment, increase action potential duration, and decrease conduction velocity in excised female rat hearts [2]. Since alterations in conduction velocity can affect ventricular pressure [3], we aimed to investigate the effect of BPA exposure on cardiac mechanical function. We hypothesized that a decrease in cardiac left ventricular pressure, due to delayed conduction velocity, could also result in decreased contractility (rate measurement of LVdP).

Analysis of Ca²⁺ transients indicated that, at high pacing frequencies, BPA exposure hinders the frequency potentiation response of cardiac tissue. Frequency potentiation is an adaptive mechanism whereby cardiac contractility increases at fast heart rates to maintain cardiac output. Cardiac contractility is dependent upon the concentration of intracellular Ca²⁺ ions that are released by the sarcoplasmic reticulum (SR) with each round of contraction. Alterations in calcium handling and contractility can impact the heart’s ability to adapt to high heart rates under exercise or stress conditions.

Discussion

The findings indicate that further studies are necessary to clarify the complete extent through which BPA affects cardiovascular function.

References


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