The cardioprotective effects of caffeic acid phenethyl ester (CAPE) on myocardial ischemia/reperfusion (I/R) injury

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INTRODUCTION

Reperfusion injury is the acceleration of heart damage which occurs during the reintroduction of coronary blood flow to a prolonged ischemic area [1]. Oxidative stress is a major cause of reperfusion injury by reducing the bioavailability of nitric oxide (NO), damaging cellular function leading to cell death/apoptosis. To date, there is no effective clinical treatment for reperfusion injury. CAPE is an active component of propolis collected from honeybee hives that exhibits both anti-oxidant and anti-inflammatory effects [2]. Recently, CAPE when given prior to ischemia was found to be cardioprotective against IR injury [3,4]. The beneficial effects of CAPE are possibly mediated by upregulating heme oxygenase-1 and/or increased bioavailability of NO. However, the effects of CAPE when given at reperfusion in myocardial IR (MI/R) injury has not been evaluated. This study tested the effects of CAPE on postreperfused cardiac function, infarct size, and putative mechanisms in an isolated rat MI/R model when given at reperfusion.

HYPOTHESIS

In this study, we hypothesized that CAPE when given at reperfusion would attenuate IR induced cardiac contractile dysfunction and infarct size. Moreover, the cardioprotective effects of CAPE may be inhibited by a non-selective NO synthase inhibitor (NG-nitro-L-arginine methyl ester (L-NAME)) or a heme oxygenase-1 inhibitor (tin protoporphyrin (SnPP)).

METHODS

Isolated Rat Heart MI/R Experiments: Hearts were isolated from male Sprague Dawley rats (275-325g, Charles River, Springfield, MA) via Langendorff heart preparation as previously described [5]. Experimental protocol is shown in Figure 2.

A pressure transducer (SPR-524, Millar Instruments, Inc., Houston, TX) was inserted into the left ventricle to record cardiac function (e.g. left ventricular end systolic and diastolic pressure (LVESP & LVEDP), respectively). Coronary flow was measured by a flow probe (T106, Transonic Systems, Inc., Ithaca, NY) which was placed in the inflow area [1]. Oxidative stress is a major cause of reperfusion injury by scavenging of NO by superoxide and/or increased bioavailability of NO. However, the effects of CAPE when given at reperfusion in myocardial IR (MI/R) injury has not been evaluated. This study tested the effects of CAPE on postreperfused cardiac function, infarct size, and putative mechanisms in an isolated rat MI/R model when given at reperfusion.

RESULTS & DISCUSSION

CAPE (n=5) restored LVDP to 85 ± 14% of baseline value at 60 min post-reperfusion compared to untreated control hearts (n=11) that only recovered to 45 ± 8% of baseline value (p<0.01).

CAPE (n=5) restored LVESP to 139 ± 14% of baseline value at 60 min post-reperfusion compared to untreated control hearts (n=11) that only recovered to 106 ± 7% of baseline value (p<0.05).

CAPE (n=5) restored dP/dtmax to 60 ± 11% of baseline value at 60 min post-reperfusion compared to untreated control hearts (n=11) that only recovered to 33 ± 5% of baseline value (p<0.05).

A non-selective nitric oxide synthase inhibitor, L-NAME (50 μM, n=5); or a heme oxygenase-1 inhibitor, SnPP (20 μM, n=5), significantly abolished the cardioprotective effects of CAPE (all p<0.05).

CONCLUSION

Our results suggest that CAPE when given at reperfusion improves post-reperfusion contractile function and reduces infarct size. The cardioprotective effects of CAPE may be mediated by increasing NO bioavailability and/or heme oxygenase-1 activity. The effects of CAPE on mitochondrial function during IR will be determined in future experiments.

REFERENCES


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