

P4.13

Role of store operated calcium and L-type calcium channels in coronary artery hypercontraction after ischemia and reperfusion process

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Rational and Aims: Calcium antagonists are used in interventional cardiology to prevent coronary vasoconstriction or to overcome the no-reflow phenomenon after primary angioplasty therapy. Coronary hypercontracture is originated by the alterations in intracellular calcium handling after ischemia and reperfusion (IR), which have an exacerbated response to agonist released by endothelium such as Endothelin. Recent evidences have highlighted the new role of store operated calcium channels (SOCC) in intracellular calcium homeostasis in coronary artery. The aim of this study was to evaluate the role of SOCC and L-type Ca²⁺ channels (LTCC) in coronary artery vasoconstriction originated by in vitro simulated ischemia and reperfusion protocol.

Methods: We used left anterior descendent coronary arterial rings (ADA) isolated from Wistar rats, to study the contractility as well as intracellular Ca²⁺ concentration ([Ca²⁺]_i) under a simulated IR protocol.

Results: First, we observed that coronary artery tone barely increased after a period of ischemia and, this small change was not maintained during reperfusion. Second, we used Endothelin to mimic the effect of agonist released during "no-reflow" phenomenon. We found that Endothelin addition during ischemia promote small [Ca²⁺]_i and coronary artery tone increase. Meanwhile, these effects were significantly potentiated during reperfusion. Interestingly, the resulting Endothelin-induced vasoconstriction and [Ca²⁺]_i increase were successfully abolished by the inhibitors of SOCC, Gadolinium, and LTCC, nifedipine.

Conclusions: Our data confirm that hypercontraction of coronary artery induced by Endothelin after a process of ischemia-reperfusion involve the activation of LTCC and SOCC.

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P4.14

Vasoactive actions of lysophosphatidic acid

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We aimed to analyze the vasoactive effect(s) of lysophosphatidic acid (LPA) in order to better understand its role in cardiovascular homeostasis. Thoracic (TA) and

abdominal aorta (AA) segments were isolated from adult male wild type and knock out mice deficient in LPA1 or LPA2 receptors, endothelial NO synthase (eNOS), cyclooxygenase-1 (COX1) or thromboxane receptors (TP). Isometric tension changes of the vessels were determined in myographs. The endothelium was mechanically removed in some segments. Expression of LPA receptors in freshly isolated mouse aortic endothelial cells (MAEC) and the vascular smooth muscle (VSM) were analyzed by quantitative real-time PCR. The vasoactive effects of LPA depended on the integrity of the endothelium: it induced relaxation in intact vessels (both TAs and AAs), whereas in the absence of endothelium or eNOS vasoconstriction developed which was more pronounced in the AA. PCR analysis revealed the presence of mRNA encoding the 1, 2, 4, and 5 subtypes of LPA receptors in MAEC while in VSM LPA1 was predominantly whereas LPA3 and LPA4 expressed at lower levels. The LPA1–3 agonist VPC31143 mimicked whereas the LPA1,3 antagonist Ki16425 inhibited all effects of LPA. In accordance, genetic deletion of LPA1 but not that of LPA2 abolished LPA-induced vasorelaxation. Inhibition of the protein kinase B/Akt pathway by wortmannin and MK-2206 failed to influence the effect of LPA, while inhibition of phospholipase C β by U73122 or edelfosine abolished LPA-induced vasorelaxation. Surprisingly, inhibition of COX by indomethacin and genetic deletion of either COX1 or TP abolished LPA- and VPC31143-evoked vasoconstriction in endothelium denuded AA segments. Our results indicate that in intact vessels LPA induces LPA1- and PLC β -dependent activation of eNOS and consequent relaxation of the VSM. In contrast, in the absence of endothelium or eNOS LPA induces vasoconstriction by activating VSM COX1 and autocrine/paracrine release of a prostanoid, presumably thromboxane A₂. This latter effect of LPA may contribute to the altered vascular reactivity in pathophysiological states associated with endothelial dysfunction.

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Cardiovascular effects of beta-carotene are lost when it was applied at high concentration

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Nowadays, there is a growing interest in compounds derived from plants as potential drug raw materials. This great interest due to the fact that substances of natural origin frequently are less toxic and have less side effects. One of the most studied compounds is beta-carotene (BC). Several clinical studies can be found having investigated the cardiovascular effects of BC, but all these results are rather controversial. There is increasing body of evidence showing that beside the well known antioxidant properties, under strong oxidative circumstances BC could be prooxidant either. We investigated the effects of long term, low- and high-dose BC treatment in ischemic/reperfused hearts isolated from healthy and ZDF rats. Rats were treated with various daily doses of BC for 4 weeks, and then hearts were isolated and subjected to 30 min

1. Dancs PT , Ruisanchez E , Balogh A , Panta CR , Miklos Z , Nusing RM , Aoki J , Chun J , Offermanns S , Tigyi G , Benyo Z
LPA1 receptor-mediated thromboxane A2 release is responsible for lysophosphatidic acid-induced vascular smooth muscle contraction
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2. Ruisanchez É , Dancs P , Kerék M , Németh T , Faragó B , Panta R , Balogh A , Tigyi G , Benyó Z

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