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Calcium oscillations and their inhibition by different drugs in human mesenteric arteries

J Navarro-Dorado[1], M Garcia-Alonso[2], M Ramajo[1], S Redondo[1,3], U Medina-Moreno[1], T Tejerina[1]. *[1]Universidad Complutense de Madrid,Facultad de Medicina, Pharmacology 28040, Spain, [2]Hospital Clinico San Carlos de Madrid, Service of General Surgery 28040, Spain, [3]Hospital Nuestra Señora de Sonsoles, Service of Haematology 05004, Spain*

Introduction: It is well documented in most experimental animal studies on intact vascular smooth muscle, that both physiological and pharmacological agonists induce oscillatory fluctuations in intracellular calcium ([Ca2+]i) to initiate and maintain vasoconstriction (Iino et al., 1994; Lee et al., 2002; Mauban et al., 2001; Peng et al., 2001; Syyong et al., 2009). However, oscillations have not yet been observed in human arteries.

Objectives: Our study was proposed to find out the existence of these oscillatory fluctuations in [Ca2+]i on human mesenteric arteries, and their possible inhibition by different drugs.

Methods: Fragments of unwanted, surplus human mesenteric tissue from patients undergoing abdominal surgery were placed in vials containing RPMI at 4ºC. The mesenteric artery was removed and cleaned of surrounding connective tissues. The vessel was cut into rings segments of 2mm in length and loaded in PSS with Fluo-4 AM. They were then inverted and isometrically mounted on a myograph on the stage of a confocal microscope for [Ca2+]i measurements. All experiments were performed at 37 ℃. Phenylephrine (phe) was added to observe the calcium movements and after 5 minutes one of these different vasodilatory drugs (Nifedipine, 2APB, HA-1077, CPA) were added to a different ring section of the artery to asses the effects on the calcium oscillations and vessel contraction.

Results: Oscillatory fluctuations in intracellular calcium ([Ca2+]i) were observed in mesenteric arteries from patients (n=9). In each patient we could observe different cells with different patterns, from almost no response to continuous oscillations. After phe-mediated contraction CPA had very variable responses relaxing completely the artery and inhibiting oscillations in just one of the n=5, meanwhile in the rest there was no relaxation and a small inhibition on the oscillations. 2APB relaxed the vessel by 82.8±3.5% (n=4), in 3 cases, it reduced oscillations, but could only totally inhibit them in one. Nifedipine relaxed the vessel by 92% and 75% on 2 different patients, inhibiting the oscillations. HA-1077 completely relaxed the vessel and totally reduced the oscillations (n=3).

Conclusions: as described previously on animals, we have observed oscillatory fluctuations in [Ca2+]i induced by pharmacological agonist (phe), that initiated and maintained vasoconstriction on human mesenteric arteries. In addition, several different vasodilating drugs with different mechanism of action have been observed to relax the arteries and inhibit the oscillations.

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Grants: FIS PI080920

RECAVA RD06/0014/1007 (Spanish Ministry of Health).