Acetylcholine Causes an Unusual Oscillatory Depolarisation and Contraction in Human Small Coronary Arteries – Role of Endothelium-Derived Relaxing Factor (EDRF)
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Acetylcholine generally causes relaxation of large and small arteries by acting on endothelial cells to release a powerful local factor, EDRF, now thought to be nitric oxide. Contraction of human large coronary arteries in response to acetylcholine has been reported but has generally been taken as evidence of endothelial dysfunction at sites of atheroma. We report here that in human coronary resistance arteries (average internal diameter = 155 \( \mu \)m) freshly dissected from the tip of the right atrial appendage, acetylcholine causes a most unusual depolarisation and oscillation of the smooth muscle cell membrane potential and contraction in the absence of any atheroma. This response pattern is dependent on Ca\(^{2+}\)ext but was unaltered by the removal of extracellular Na\(^+\) or by high concentrations of the dihydropyridine L-type Ca\(^{2+}\) channel inhibitor, felodipine (0.1 \( \mu \)M). The endothelium was mostly intact as judged by morphology. In addition, the EDRF-releasing agent, substance P, repolarised and relaxed the artery in the presence of acetylcholine. By contrast, in resistance arteries from human skin, acetylcholine only caused hyperpolarisation and relaxation. These studies suggest that the human coronary resistance arteries from elderly cardiac patients are unusually excited by muscarinic receptor stimulation and emphasise the capacity of EDRF to antagonise membrane depolarisation and contraction.

Diosmin Therapy Modifies the Metabolism of Noradrenaline by the Varicose Human Saphenous Vein
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We have previously shown [Araújo and Osswald, Phlebology, p. 666, 1989] that diosmin 30-100 \( \mu \)mol/l reduces the metabolism of noradrenaline (NA) in fragments of varicose saphenous veins obtained at surgery. Since diosmin is widely used in patients with chronic venous insufficiency we decided to test if the drug, administered in therapeutic doses, would affect NA metabolism in the veins of the patients so treated. Sex- and age-matched patients in which surgery was indicated were allocated at random to control (n = 5) and treated groups (n = 6; 600 mg b.i.d. p.o. during 10 days). Fragments of saphenous vein were incubated with \(^{3}\)H-NA 0.2 \( \mu \)mol/l during 60 min; interval between operation and incubation was less than 30 min. Column chromatography and liquid scintillation counting were used to measure \(^{3}\)H-NA and its metabolites. In the treated group, accumulation of \(^{3}\)H-NA was significantly reduced and the formation of metabolites approximately halved. The present results show that oral administration of diosmin has evident effects on the in vitro metabolism of NA in varicose venous tissue.
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