Altered reactivity to norepinephrine through COX-2 induction by vascular injury in hypercholesterolemic rabbits

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Although long term use of cyclooxygenase (COX)-2 inhibitors may be associated with increased cardiovascular risk, their effects on vascular reactivity in atherosclerosis has remained largely unexplored. The aim of the present study was to evaluate the role of COX-2 induced by an atherosclerotic process, in the local control of vascular tone. To this end, New Zealand White rabbits were fed 0.3% cholesterol for 3 weeks before being subjected to balloon injury of the abdominal aorta. After another 2 weeks, the aorta was removed and used for organ bath experiments and immunohistochemistry, and the prostaglandins released were measured using enzyme immunoassays. Hypercholesterolemia and vascular injury significantly increased the thickness of the intimal layer, which was associated with an induction of COX-2 immunoreactivity throughout the aortic wall. In these preparations, a significant decrease of the maximal contractions induced by norepinephrine was observed: 89.3±12 mN in controls (n=5) versus 67.6±13 mN in balloon injured aortas from hypercholesterolemic rabbits (n=5); P<0.05. The norepinephrine-induced contractions of atherosclerotic preparations were restored by the COX inhibitors DuP-697 (0.5 μmol/L) and indomethacin (1.7 μmol/L), to similar contractions as was observed in aerobic preparations derived from healthy rabbits. Norepinephrine stimulation of the abdominal aorta was accompanied by increased levels of prostaglandin I\(_2\) in ath- ersclerotic (1.39±0.11 μg/mg, n=3) compared with normal aorta (0.53±0.17 μg/mg, n=3; P<0.05). Selective COX-2 inhibition significantly decreased the prostag- landin I\(_2\) release from atherosclerotic aorta, but had no effect on the prostag- landin release from aerobic preparations derived from normal rabbits. These observations suggest that the local induction of COX-2 during atherosclerosis decreased the sensitivity to norepinephrine, and that COX-2 inhibitors may locally increase vascular reactivity at sites of atherosclerotic lesions.

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PON1-Q192R gene polymorphism and myocardial infarction in tunisian population

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Background: Paraoxonase (PON1), an enzyme closely associated with high-density lipoproteins, appears to exert an important antioxidant effect by removing lipid peroxidation products. PON1 may also play a role in the pathogenesis of arterial thrombosis and atherosclerosis. The PON1 gene poly- morphism involves a Gln → Arg interchange at codon 192 defined by a low- activity isofrom (Q allele) and a high-activity isofrom (R allele) and has been related in some studies to myocardial infarction (MI). The purpose of the present study was to assess the relationship between PON1-192 polymorph- ism, and myocardial infarction in Tunisian population.

Material and method: A total of 303 Tunisian patients with MI and 408 healthy controls were included in the study. Diagnosis of MI was confirmed according to the European Society of Cardiology criteria. The PON1-Q192R genotypes were determined by polymerase chain reaction (PCR) amplification and restriction analysis.

Results: The genotypes frequencies were in agreement with those pre- dicted by the Hardy-Weinberg equilibrium in MI patients (X\(^2\)=5.52; p=0.63) and controls (X\(^2\)=3.26; p=0.127). A significant difference in genotype distribution and allele frequency was observed between patients and controls. Patients with MI had a frequency of 17.1 % for RR genotype, 41.1% for the QR genotype and 41.7% for the QQ genotype. The controls had a frequency of only 10.9% for the RR genotype, 37.4% for the QR genotype and 51.6% for the QQ genotype. The controls had a frequency of 17.1 % for RR genotype, 41.1% for the QR genotype and 41.7% for the QQ genotype. The controls had a frequency of 17.1 % for RR genotype, 41.1% for the QR genotype and 41.7% for the QQ genotype.