Activity of metalloproteinase-9 is related to oxidative stress in the acute coronary syndrome

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Background: Metalloproteinases (MMPs) are proteolytic enzymes, that participate in atherosclerotic plaque instability. In cellular cultures, metalloproteinases-2 and -9 (MMP-2 and MMP-9) activities increase in exposure to free oxygen derived radicals. However, in patients with acute coronary syndrome (ACS), the association of metalloproteinase activity and oxidative stress (OS) has not been studied.
Aim: To evaluate the relation between matrix metalloproteinase activity and OS in the ACS.
Methods: We studied prospectively 46 patients with non-ST segment elevation ACS, TIMI risk score ≥ 3 and ischemic electrocardiographic changes or elavated levels of Troponin I. We measured plasma activities of MMP-2 and MMP-9 (by gel zymography), malondialdehyde (MDA) (by tyobarbituric acid reactive substances) and high sensitive C reactive protein (hsCRP) (by ELISA), at admission to the coronary unit and at day five. As a control group we determined MDA levels and MMP-9 activities in plasma of 12 normal volunteers. Statistical analysis was performed using t Student test and Pearson's lineal correlation.
Results: Thirty seven patients (80%) were male, mean age 61 ± 12 years old (38 - 85 years), all of them with Troponin I elevation. The median TIMI risk score was 4 (3 - 7). 85% presented hsCRP elevation at admission (15 ± 28.7 mg/L) that increased at day 5 (35.3 ± 38 mg/L). MDA plasma levels were increased at admission vs. controls (1.54 + 0,75 μM/L vs. 0.71 ± 0.7 μM/L, $p < 0.0001$) and diminished at day 5 to a 66% of the initial value ($p < 0,0001$). MMP-9 activity was increased at admission (137 ± 64% $p < 0.0001$) and decreased at day five to a normal value (104 ± 68%, $p<0001$). No significant elevation in MMP-2 activity was found at admission nor at day five (110 ± 79%, $p = 0.06$ and 97 ± 62%, $p = 0.46$ respectively vs. controls). A significant positive correlation was found between the percentual decreases of MDA levels and MMP-9 activities at day five ($r = 0.43$, $p<0.0001$).
Conclusions: In patients with ACS we observed an early increase in inflammation, MMP-9 activity and OS. The correlation demonstrated between MMP-9 activity and OS suggests a common role of both phenomena in the pathophysiology of the ACS.