INTRAPERICARDIAL DELIVERY OF THROMBIN INDUCES ANGIOGENESIS IN A RABBIT MODEL OF CHRONIC MYOCARDIAL ISCHEMIA

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Introduction

Thrombin has been reported to be a key regulator of angiogenesis. It interacts with vascular cells, it activates or up regulates several vascular regulatory proteins and growth factors and protects endothelial cells from apoptosis. We examined the ability of thrombin, upon pericardial administration, to induce angiogenesis in a rabbit model of chronic myocardial ischemia.

Methods

A rabbit model of chronic myocardial ischemia was established by endovascular occlusion of left anterior descending coronary artery with a microcoil. On 14th postinfarct day, 2500iu thrombin (group A, n=8) or an equal volume of saline (group B, n=8) was administered intrapericardially. Four weeks after thrombin/saline administration, the animals were euthanized. Myocardial infarction was confirmed by ECG, cardiac enzymes and histopathological analysis. Left ventricular end-diastolic pressure (LVEDP) was recorded for the assessment of cardiac function. Histopathological analysis, immunohistochemical staining for the endothelial marker CD31 and electron microscopy was performed on excised hearts.

Results

Both groups showed increased serum troponin levels, ST segment elevation and histopathological changes of myocardial infarction. Animals treated with thrombin (group A), showed significantly higher vascular density in the border zone, as evaluated by CD31 immunohistochemistry, compared to the control group (group B), (41.5±40.9 vs 12.9 ± 5.6, p=0.036). The thrombin treated group also showed a significant reduction in LVEDP on the day of euthanasia compared to the 14th post-infarct day (7.2±1.7mmHg vs 12.9±2.3mmHg, p=0.012).

Discussion

A single intrapericardial administration of thrombin seems to promote formation of mature functional blood vessels and to improve cardiac function in a rabbit model of chronic myocardial ischemia. This may constitute a novel safe strategy for achieving optimal therapeutic angiogenesis.