A study of endothelins and endothelin receptors in rheumatic mitral valves


Introduction: Rheumatic fever represents a serious public health problem in Brazil, with thousands of new cases each year. It is an inflammatory and autoimmune disease, which occurs in response to infection by Streptococcus A group. The aim of this study was to evaluate the immunolabeling for ET-1, ET-A and ET-B receptors in rheumatic mitral valves. Methods: This study focused in quantitative immunoreactivity of ten mitral valves which were collected at a hospital in Aracaju, SE, Brazil. The quantitative analysis of the immunocytochemistry area of each receptor in relation to the total area of each slide was performed by ImageJ software. Statistical analysis was performed using measures of central tendency and standard deviation. In inferential analysis, we used the Pearson partial correlation (R), with significance level of <0.05. Results: In 10 samples, immunohistochemical expression for ET-1 and for its receptors was observed in eight and seven samples, respectively. In quantitative analysis, it was observed that the average area of immunoreactivity of ten mitral valves which were collected at a hospital in Aracaju, SE, Brazil. The quantitative analysis of the immunocytochemistry area of each receptor in relation to the total area of each slide was performed by ImageJ software. Statistical analysis was performed using measures of central tendency and standard deviation. In inferential analysis, we used the Pearson partial correlation (R), with significance level of <0.05. Results: In 10 samples, immunohistochemical expression for ET-1 and for its receptors was observed in eight and seven samples, respectively. Conclusion: The strong positive correlation between endothelin receptors indicates that both have a role in the pathophysiology of rheumatic mitral stenosis.

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Estrogen A receptor blockade and long term outcome in patients with ST elevation acute coronary syndrome

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Background: ST-elevation acute coronary syndrome (STE-ACS) is characterized by thrombotic coronary occlusion compromising blood flow at the epicardial and microvascular levels. Coronary thrombi are a source of large amounts of endothelin-1 (ET-1), a pro-fibrotic vasocostrictor and a mediator of microvascular dysfunction and cardiac remodeling. Methods: Patients with posterior-wall STE-ACS were randomly assigned to intravenous BQ-123 or placebo as described elsewhere (n = 54). During a three-year follow-up period, patients were followed and kept on optimal medical treatment by an investigator who was blinded to the acute treatment allocation. Results: During the median follow-up period of 3.3 years (IQR 2.9–3.7), no deaths occurred. The reasons for rehospitalisation (n = 19) were unplanned coronary revascularization (n = 10, 52%), worsening angina (n = 3, 17%), hypertensive urgency (n = 2, 11%), as well as stroke (n = 1), dyspnoea (n = 1), ventricular tachycardia (n = 1) and cerebrovascular disease (n = 1). We observed a longer event-free survival in patients randomized to receive BQ-123 compared to controls (n = 54). Conclusion: Estrogen A receptor blockade is associated with reduced big-endothelin level after experimental cardiac tamponade

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Objective: Cardiac tamponade is a severe clinical syndrome most often caused by high-energy thoracic injuries. Following tamponade, the release of vasoconstrictive mediators contributes to circulatory redistribution, leading to peripheral macro- and microcirculatory complications including gastrointestinal hypoperfusion. As a consequence of hypoxia the complement system is activated and anaphylatoxin C5a may be produced. Our aim was to investigate the modulator effects of complement C5a antagonist (C5aA) treatment on the endothelin system and the accompanying circulatory and inflammatory changes in a large animal model of experimental cardiac tamponade. Methods: In anaesthetized, ventilated and thoracotomized minipigs (n = 7) tamponade was induced for 60 min by intrapericardial fluid administration, meanwhile the mean arterial pressure (MAP) was reduced to 40–45 mm Hg. Group 2 was treated with C5aA (AcPepA, Nagoya, Japan) at the 45th min of tamponade (4 mg/kg iv; n = 6), while group 3 (n = 6) served as sham-operated control. Macrophomedemics were monitored for 240 min, whole blood superoxide production, plasma HMGB-1 and big-endothelin (big-ET) levels, small intestinal myeloperoxidase (MPO) activity were measured. Average red blood cell velocity (a-RBCV) in the small intestinal mucosa was determined by intraleral orthogonal polarization imaging (OPS) technique. Results: After tamponade plasma levels of big-ET were increased together with superoxide production, HMGB-1 levels and MPO activities. The C5aA treatment normalized the macrohemodynamics, and besides the a-RBCV was increased, SOX, HMGB-1, MPO and big-ET levels were reduced. Conclusion: These results demonstrate the possible connections between the activation of complement- and endothelin systems, and the potential for C5aA to decrease the potentially harmful inflammatory consequences of experimental cardiogenic shock. Grant supports: OTKA-K104569; TAMOP-4.2.2.A-11/1-KONV-2012-0035; TAMOP-4.2.2.A-11/1-KONV-2012-0073; TEJ-JP-16-09.

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