

Oral treatment with a zinc complex of acetylsalicylic acid prevents diabetic cardiomyopathy in a rat model of type 2 diabetes

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Introduction Type 2 diabetic patients are at an increased risk of cardiomyopathy and heart failure is a major cause of death amongst these patients. Growing evidence indicates that proinflammatory cytokines can cause sustained development of insulin resistance and anti-inflammatory medications may reverse this process.

Hypothesis We investigated the effects of an oral administration of zinc and acetylsalicylic acid in the form of bis(aspirinato)zinc(II) complex Zn(ASA)₂ on different aspects of cardiac damage in the Zucker diabetic rat (ZDF), an experimental model of type 2 diabetic cardiomyopathy.

Methods The nondiabetic control and the diabetic ZDF rats were pretreated orally with a vehicle or Zn(ASA)₂ for 24 days. At the age of 30–32 weeks, both the electrical activity and the left ventricular (LV) structural/functional parameters were assessed via electrocardiogram and pressure volume (PV) conductance catheter system.

Results The Zn(ASA)₂ treatment significantly decreased the blood glucose concentration (39.6±3.1 vs 50.4±2.6 mM), normalized the impaired LV contractility index ($E_{\max}$ 3.7±0.4 vs 1.9±0.6 mmHg/μl), the passive LV stiffness (end diastolic PV relationship: 0.064±0.008 vs 0.084±0.014 mmHg/μl), and the diastolic dysfunction (LV end diastolic pressure: 6.5±0.6 vs 7.9±0.7 mmHg). Furthermore, the ECG revealed a restoration of the prolonged corrected QT intervals (63±3 vs 83±4 ms, $p<0.05$) by Zn(ASA)₂. A histological examination revealed an increase in the cardiomyocytes transverse cross section area in diabetic rats compared to the controls, which was significantly decreased after treatment with Zn(ASA)₂. Furthermore, a significant increase in fibrotic formation was observed in the diabetic rats compared to controls, and Zn(ASA)₂ administration showed similar collagen content in the ZDF+Zn(ASA)₂ rats and in the nondiabetics. A significant increase in the density of TUNEL positive cell nuclei in the diabetic hearts, indicating DNA fragmentation, was significantly decreased by Zn(ASA)₂. Additionally, in the diabetic hearts, Zn(ASA)₂ significantly decreased nitrotyrosine formation.

Conclusions The oral administration of Zn(ASA)₂ may have therapeutic potential with the aim of preventing cardiac complications in type 2 diabetic patients.