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Research Article

Effects of high and low salt intake on left ventricular remodeling after myocardial infarction in normotensive rats

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Abstract

The dietary–sodium restriction is a standard approach following an acute myocardial infarction (MI). We examined the hypothesis in which the use of a high or low–sodium diet would worsen post–infarction left ventricular remodeling in rats and facilitate the development of heart failure. Left coronary artery ligation or sham–operated (SO) was produced in male Wistar rats (250–290 g). After surgery, animals were assigned to one of the three diets: standard amount of sodium (0.3% NaCl, SO and MI groups), a high–sodium diet (0.6% NaCl, SO–High and MI–High groups), or a low–sodium diet (0.03% NaCl, SO–Low and MI–Low groups). Diets were provided for 8 weeks post–surgery. Mortality rate was elevated in high–salt group (MI–Low, 21.4%; MI, 35.3%; MI–High, 47.6%). Contractility parameter was seen to be impaired in MI–Low animals (3195 ± 211 mm Hg/s) compared with MI (3751 ± 200 mm Hg/s). Low–salt diet did not prevent myocardial collagen deposition (MI–Low, 5.2 ± 0.5%; MI, 5.0 ± 0.4%) nor myocyte hypertrophy (MI–Low, 608 ± 41μ^2; MI, 712 ± 53 μm^2) in left ventricle after MI. High–salt intake increases collagen volume fraction (SO, 3.3 ± 0.4%; SO–High, 4.7 ± 0.4%) in animals sham, but no major changes after MI. Our results show that ventricular remodeling was not altered by immediate introduction of low sodium after MI, and it may be a safe strategy as a therapeutic intervention to avoid volume retention. However, high sodium can be harmful, accelerating the post–infaction ventricular remodeling. J Am Soc Hypertens 2015;9(2):77–85.

Keywords: Cardiac fibrosis; diet; heart failure; sodium consumption.

Introduction

Excessive salt intake has been extensively linked to cardiovascular morbidity and mortality. Over the last decades, clinical and experimental studies have shown that increased salt intake is associated with deleterious effects, including endothelial dysfunction, hypertension, stroke, heart failure, and kidney disease.[1–3] Thus, high salt intake has been considered a powerful risk factor for cardiovascular disease (CVD).

Most population–based studies have found that salt consumption currently exceeds acceptable levels established by regulatory agencies.[4] In fact, current recommendations advocate a reduction in salt intake to reduce the incidence of CVD, the most frequent cause of death worldwide. However, some authors have raised a number of issues about the current recommendations for a significant reduction in salt intake in the general population.[5,6] It has been argued that low–salt diets may activate the sympathetic nervous system and the systemic renin–angiotensin–aldosterone system (RAAS), two effects that should be avoided during the post–infarct period because of their deleterious effects on left ventricular remodeling. Thus, low–salt diets could potentially be harmful after infarction because cardiac hypertrophy and fibrosis may facilitate the development of heart failure.

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Acute myocardial infarction (MI) is an extreme situation that is associated with complex changes in cardiac architecture and function that result in a high mortality rate. This process of change in the infarcted heart is known as myocardial remodeling, and it progressively leads to heart failure.[7] It is noteworthy that, aside from standard pharmacologic approaches, a reduction in sodium intake is one of the first therapeutic actions after acute myocardial infarction. Based on the well–known effects of high salt consumption, it is expected that reducing salt intake after MI would attenuate left ventricular remodeling, thus preventing heart failure. However, this hypothesis has not been confirmed. For instance, Klein et al[8] and Paterna et al[9] did not observe beneficial effects after lowering sodium intake in heart failure patients. Instead, they observed increased hospitalization times for cardiovascular causes, increased mortality rates,[8] and detrimental renal and neurohormonal effects.[9] Thus, we sought to determine whether strict salt restriction or increased consumption of salt would affect the mortality rate and ventricular remodeling after acute MI in rats.

Materials and Methods

Animals

Male Wistar rats (260–290 g) from the animal core facility of the Federal University of Espirito Santo were used in the experiments. The animals were housed in appropriate cages in a room with controlled temperature and with a 12 hour light:12 hour dark cycle. Animals had free access to rat chow and tap water. All procedures were conducted in accordance with the Guide for the Care and Use of Laboratory Animals (NIH publication N. 85–23, revised 1996) and approved by the institutional Committee for Ethics in Animal Research (CEUA–UFES n. 068/2012).

Coronary Artery Occlusion and Groups

MI was induced as described previously.[10] Briefly, the animals were anesthetized with ketamine (50 mg/kg intraperitoneal [ip]; Agener União) and xylazine (Bayer; 10 mg/kg, ip), and left thoracotomy was performed in the fourth intercostal space. The heart was exposed rapidly, and the left coronary artery was permanently occluded using 6–0 monofilament nylon sutures. The thorax was closed, and the animals recovered normal respiratory movements. Sham–operated (SO) rats that underwent the same surgical procedures except coronary ligation were used as non–infarcted control animals. Immediately after surgery, the animals were randomly assigned into six groups to receive a diet containing the standard amount of sodium (0.3% NaCl, SO and MI groups), a high–sodium diet (0.6% NaCl, SO–High and MI–High groups), or a low–sodium diet (0.03% NaCl, SO–Low and MI–Low groups).

Diets were specifically prepared for this project, and all components of the rats' diets were held constant except the sodium content. The animals were maintained on one of the three experimental diets for 8 weeks.

Noninvasive Blood Pressure Measurement

Systolic blood pressure was recorded by noninvasive tail cuff plethysmography before surgery and 30 and 60 days after surgery. Briefly, the rat was placed in a pre–warmed restraining chamber, and occluding cuffs and pneumatic pulse transducers were positioned on the rat's tail. The cuff was inflated and deflated automatically, and the signal was automatically collected in an IITC apparatus (IITC Inc).[11] Five blood pressure measurements were made for each rat, and the mean of these measurements was recorded.

Physiological Parameters

Each rat's body weight was measured before surgery and then once per week. To determine the food and water intake and urinary parameters for each rat, the animals were placed into individual metabolic cages (Tecniplast 304) for 2 consecutive days 60 days after surgery. The first day was used as an adaptation period; 24–hour food and water consumption, as well as urine production, were measured during the second day. The urine production was used to measure the urinary excretion of sodium (MH-LAB ISE Electrolyte Analyzer, Diamond Diagnostics Inc).

Hemodynamic Measurements

At the end of the 8–week follow–up period, the animals were anesthetized with ketamine (50 mg/kg ip) and xylazine (10 mg/kg ip). The right common carotid artery was catheterized with a fluid–filled polyethylene catheter (P50) connected to a pressure transducer (TRI 21, Letica Scientific Instruments) and to a digital system (Powerlab/4SP ML750, ADInstrument) to record the pulsatile blood pressure. The catheter was then advanced into the left ventricular cavity to record intracavitary pressure and its first temporal derivative. Left ventricular peak systolic pressure (LVSP) and end–diastolic pressure (LVEDP) and the maximum positive and negative values of dP/dt (+dP/dt max and −dP/dt max) were recorded under regular rhythm with 1–kHz filtering.[12]

After hemodynamic recordings, the naso–anal length of the animal was measured, and the animal was euthanized with an overdose of anesthetic medication. The heart was rapidly removed, flushed in cold saline solution, dried with filter paper, weighed, and fixed in a buffered solution of paraformaldehyde (4%, pH 7.4) for subsequent histologic analysis. The lungs, kidney, liver, and the gastrocnemius muscle were also removed and weighed.