EFFECT OF INFECTION ON CARDIAC AND SKELETAL MUSCLE CALCIUM CONTENT

IN THE RAT ENDOCARDITIS MODEL

L.M. Baddour, M.M. Hill, A.B. Hinton and G.M.A. Palmieri
Department of Medicine, University of Tennessee-Memphis
Memphis, TN 38163

There is a 10,000 fold gradient of Ca across the plasma membrane of every cell. The Ca concentration in the extracellular compartment is $10^{-3}M$ and only $10^{-7}M$ in the cytosol. Under normal circumstances, this gradient is tightly maintained by the very low permeability of plasma membranes for Ca. In some diseases, however, there is a loosening of this control and Ca intrudes into the cell causing reversible or irreversible cell damage. Elevation of cytosolic calcium, reduces ATP synthesis depriving the cell of the energy needed for maintaining its normal functions (1,2). Thus the efficiency of the Ca pumping mechanisms decreases, resulting in additional cellular Ca accumulation, causing more cell damage. High cytosolic Ca also causes cell injury and eventual cell death by stimulation of Ca-activated neutral proteases (3,4) and phospholipases (5,6).

Alterations of cellular Ca homeostasis plays a role in the pathogenesis of a variety of human disorders. In some, such as Duchenne muscular dystrophy, there is a genetic structural defect of plasma membranes that allows an exaggerated influx of Ca into muscle cells. In other diseases, such as acute pancreatitis, the defect is acquired. This subject was recently reviewed by Rasmussen and Palmieri (7).

Hypocalcemia may occur in severe infections, particularly in septic shock (8). Zaloga and Chernow (9) found reduced blood Ca$^{2+}$ in 12 of 60 patients with septic shock. Although, some alterations in calcitropic hormones were observed in those patients, there is no definitive explanation for the acute hypocalcemia in sepsis. The possibility that excessive translocation of calcium into the cellular compartment may occur in infection has not been explored. We therefore tested this hypothesis in the rat model of experimental endocarditis.

Methods: The procedure used to produce endocarditis in rats has been previously described in detail (10). Briefly, an intracardiac catheter is placed in the left ventricle, via the right common carotid
artery, of 150-200g Sprague-Dawley rats. Two days later, $10^7$ colony-forming units of Staphylococcus epidermidis suspended in 1ml of 0.15M Nace solution is injected through the tongue vein of animals. Ninety six hours after bacterial challenge, samples of the right ventricle and rectus femoris were obtained for chemical analysis. The aorta and left ventricle were opened and vegetations were excised, weighed and homogenized. The vegetations and catheters were cultured in broth. In addition, quantitative cultures of the vegetation suspensions were performed. No gross abnormalities were observed in the right ventricle which was not catheterized in these experiments. Control rats were subjected to identical procedures, but sterile saline solution instead of bacterial inocula was injected. Calcium was measured in acid extracts of dry, defatted samples of right ventricle and rectus femoris as previously reported (11,12).

Results: There was similar tolerance to the procedures in infected and control rats. A significant increase ($p=0.01$) in Ca content in the right ventricle of infected animals (Table 1) was observed. The Ca content of the rectus femoris of infected rats was elevated in several animals, but as a group it did not show statistical significance.

Table 1. Muscle Ca* in Endocarditis Content in Infected and Noninfected Rats.

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<tr>
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<th>Right Ventricle (n)</th>
<th>Rectus Femoris (n)</th>
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<tr>
<td>Control (4)</td>
<td>32.49 ± 6.39</td>
<td>(6) 23.71 ± 2.37</td>
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<tr>
<td>Infected (12)</td>
<td>72.51 ± 12.58</td>
<td>(12) 51.90 ± 16.04</td>
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*p=0.01
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Discussion: This preliminary observation clearly demonstrates that rats which develop experimental endocarditis due to S. epidermidis have a marked increase in the Ca content of the right ventricle. The skeletal muscle also showed some increment in calcium accumulation. In choosing the present experimental model, we avoided the technically simpler intraperitoneal bacterial inoculation model. The intraperitoneal infection could have caused peritonitis and pancreatitis, and prior studies of noninfectious acute pancreatitis have demonstrated elevated skeletal muscle Ca by 100% in dogs (13).

Since the relatively mild infection in the present study caused a 120% increment in the myocardium of the right ventricle, it is conceivable that the hypocalcemia of septic shock could be explained, in part, by an excessive translocation of Ca from the extracellular to the intracellular compartment. Parathyroid hormone (PTH) could accentuate the cellular damage caused by excessive intracellular Ca during infection by stimulating Ca entry into cells (14). Although this hypothesis needs to be explored, it is tempting to speculate that suppression of PTH secretion by maintaining an adequate intake of Ca could be beneficial during infection, since Wood (15) reported more than 150 years ago that administration of Ca had a positive effect in the treatment of tuberculosis. Moreover, vitamin D promotes antituberculosis resistance (16), and calcitriol stimulates macrophages-induced

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