Is parathormone a cardiac toxin in uremia?

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Abstract

In uremia, parathormone (PTH) has been associated with inadequate left ventricular hypertrophy, cardiomyopathy, and mitral anular calcification (MAC). We related levels of serum PTH, calcium, phosphate, magnesium, calcium-phosphate product, and systolic blood pressure to average left ventricular wall thickness, left ventricular mass index, ejection fraction, and presence and extent of MAC by echocardiography in 44 patients before and after renal transplantation.

Pre-transplant, 18 patients (41%) had MAC; these and the 26 others had similar values for serum PTH, calcium-phosphate product, systolic blood pressure, age, and years of hemodialysis. The patients with PTH levels greater than 1000 mcl eq/ml had higher systolic blood pressures pre-transplant (157 ± 21 vs 147 ± 17 mm Hg, p<0.05), but not post-transplant as PTH levels normalized.

Post-transplant, there were significant decreases in left ventricular mass index (140 ± 35 to 103 ± 25 g/m²) and average diastolic left ventricular wall thickness (1.4 ± 0.2 to 1.2 ± 0.2 cm, both p<0.05); however, ejection fraction and extent of MAC did not change. Left ventricular mass index, average diastolic left ventricular wall thickness, and ejection fraction did not correlate with serum PTH or electrolyte levels before or after renal transplantation.

MAC is present in more than one third of uremic pts and does not resolve after renal transplantation. Although PTH does not correlate with left ventricular hypertrophy, cardiac function, or MAC before or after transplantation, elevated levels pre-transplant are associated with a slightly greater degree of hypertension. Thus PTH may be a mild vasoactive pressor in some patients with end-stage renal failure.

Introduction

Parathyroid hormone (PTH) has been reported to be a significant factor in the development of vascular and myocardial disease in patients with primary or secondary hyperparathyroidism [1]. Since serum levels of PTH are extremely elevated in renal failure, this hormone has been implicated in the development of mitral anular calcification (MAC) [2–4], ‘uremic cardiomyopathy’ [5], and ‘inadequate left ventricular hypertrophy’ [6]. We have previously reported a significant decrease in left ventricular mass and volume by echocardiography after renal transplantation [7]. In order to further determine whether left ventricular hypertrophy, left ventricular function, and cardiac calcification in renal transplant patients could be more definitively related to PTH, calcium, phosphate, and magnesium levels, we analyzed cardiac and metabolic evaluations before and after renal transplantation in these patients.

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Methods

From the overall adult population of 849 renal transplantations performed over a 5.4 year period (July 1982 to November 1986), adult patients with end-stage renal failure who had echocardiograms within 2 weeks of renal transplantation were entered into the study. Patients were asked to return for follow-up echocardiograms in 1987, which were performed at various periods of time after renal transplantation. Patients with a history of myocardial infarction, valvular disease, or transplant rejection leading to loss of graft function were excluded.

Hospital and transplant clinic charts of study patients were reviewed for the following: 1) serum PTH values during a 6 month period prior to renal transplantation and during the follow-up period, 2) similar preoperative and postoperative values for serum calcium, phosphate, magnesium, albumin, and alkaline phosphatase, 3) years of hemodialysis, 4) years of hypertension by patient history or duration of antihypertensive drug therapy, 5) blood pressure values in the preoperative, immediate postoperative, and follow-up periods, and 6) heights and weights at the times of echocardiography.

Calcium was determined by an atomic absorption spectroscopy technique [8]. Corrections in serum calcium were made for reductions in serum albumin; the correction was performed for metric units and then converted to SI units: ‘corrected calcium’ = uncorrected calcium + 1.8 × (4.0 - mean serum albumin). The calcium-phosphate product was defined as the product of mean corrected serum calcium and mean phosphate. Serum PTH was determined by the method of Arnaud [9], a C-terminal radioimmunoassay that has a coefficient of variability of 12%.

Chest radiographs were reviewed by a skeletal radiologist (CAH) for evidence of cardiac calcification and renal osteodystrophy. The radiologist had no knowledge of the echocardiographic or laboratory evaluation.

Echocardiography was performed on an Irex Meridian® (Ramsey, New Jersey) using a 3.5 MHz transducer with patients positioned at 90° left lateral decubitus. All standard two-dimensional views were recorded, including parasternal long and short axis at the level of the mitral anulus, apical two and four chamber, and supine subcostal views. Prior to recording, gains were optimized, chamber sizes were maximized, and respiration was suspended.

Left ventricular mass was calculated using a truncated ellipsoid formula [10-11]. Left ventricular mass index was determined by dividing left ventricular mass by body surface area. By subtracting left ventricular short axis endocardial area from epicardial area, average diastolic wall thickness was computed at the level of the tips of the papillary muscles [10]. Papillary muscles were considered part of the left ventricular chamber, and were excluded from the planimetered endocardial area. In this laboratory, the upper limits of normal for average diastolic wall thickness by this technique is 1.2 cm.

Left ventricular ejection fraction was measured using a modification of Simpson’s rule [12-13]. End systolic and end diastolic endocardial areas were traced in the apical two and four chamber views.

Echocardiograms were reviewed for intensity and distribution of MAC by a blinded observer. The mitral anulus was defined as the posterior area of the atrioventricular ring, extending approximately from 3 o’clock laterally to 10 o’clock inferiorly [14-15]. The following grading scale was employed: 0 (absence of MAC), 1+ (trivial, only patchy areas of thickening in the anulus), 2+ (mild, calcification limited to less than one third of the anulus), 3+ (moderate, involving greater than one third of the anulus, or demonstrating ultrasound shadowing), and 4+ (severe MAC, involving the entire inferior aspect of the anulus).

Statistical methods included the student’s t-test and linear regression analysis. The null hypothesis was rejected at the 5% level. Results are given as mean ± SD.

Results

There were 44 patients who underwent noninvasive evaluations before and after successful renal transplantation. Average age was 40 ± 13 years at