Comparison of Parathyroid Hormone in Angiographically-demonstrated Coronary Artery Disease Patients and Healthy Thais

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Abstract

Parathyroid hormone (PTH) influences the calcium metabolism. The idea of cardiovascular effects of PTH is not new. Target cells for PTH are cardiomyocytes and smooth muscle cells. Evidence from previous studies suggest that many patients with heart disease have elevated PTH concentrations. Our objective was to determine PTH status in patients with coronary artery disease (CAD). We compared intact PTH levels in 109 CAD patients with 103 healthy people by electrochemiluminescence immunoassay. Mean values of PTH in healthy Thais and CAD patients were 37.4 ± 17.9 and 40.2 ± 21.8 respectively. No statistical difference was shown. In addition, we compared PTH levels among various numbers of coronary occlusion and also found no differences. We propose that intact PTH concentrations in CAD patients are not higher than in the healthy population.

Key word : Coronary Artery Disease, Parathyroid Hormone

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Parathyroid hormone (PTH) is a peptide hormone that is secreted from the parathyroid gland and acts on many sites. Bones and kidneys are classic target organs. PTH may also affect the function of the brain, heart, smooth muscles, lungs, erythrocytes, lymphocytes, pancreas, adrenal glands and testes[1].

Cardiovascular actions of PTH have been reported since 1925 and gained increasing interest in the eighties. PTH has several actions on the cardiovascular system[2,3]. This hormone acts on cardiomyocytes and vascular smooth muscle cells. It has effects on vasorelaxation, contractile function and heart rate. It increases the heart rate indepen-

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dent of autonomic reflexes. Patients with hyperparathyroidism are more likely to have hypertention and congestive heart failure than control subjects[4]. Few studies have shown that about 20-30 per cent of patients with congestive heart failure had elevated serum PTH[5,6]. In cases of coronary artery disease (CAD), PTH may play a potential role in arterial calcification because it is one of the osteoregulatory factors. In this study, we evaluated a group of patients with CAD to compare PTH with healthy controls.

MATERIAL AND METHOD

Study Populations

The authors studied 109 CAD patients who attended Her Majesty Cardiac Center at Siriraj Hospital between January 1998 and February 1999: 75 were men, and 34 were women. Exclusion criteria included pregnancy, renal disease and long term steroid therapy. These patients consisted of 32 unstable angina pectoris and 77 stable angina pectoris. Coronary artery lesions were angiographically verified in all cases. One hundred and three blood donors were used as control subjects: 46 were men and 57 were women.

Parathyroid Hormone

Clotted blood was collected and centrifuged at 3,000 g for 15 minutes. The serum was separated and stored at $-70^{o}C$ until analysis.

Serum concentration of intact PTH was determined by using Elecsys PTH immunoassay (Roche Diagnostics, Switzerland) which recognized intact PTH. This electrochemiluminescence immunoassay employs a sandwich test principle in which a biotinylated monoclonal antibody labeled with ruthinium complex reacts with the C-terminal fragment. The epitopes recognized by the antibodies correspond to the amino acid regions 26-32 and 55-64. Measuring range was 1.20-5000 pg/mL.

Coronary Angiography

Coronary angiography was performed on 109 CAD patients. Ninety-six of these had at least 1 diseased coronary artery, defined as a reduction of the vessel diameter of at least 50 per cent, and thirteen had normal coronary arteries.

Statistical Analysis

The StatView (Abacus, USA) program was used for statistical analysis. Unpaired *t* test was employed for analysis. Continuous values were expressed as mean $\pm$ standard deviation (SD). A p value of less than 0.05 was regarded as a significant level.

RESULTS

In the study of PTH, total calcium, and phosphorus in 103 healthy adults, distributions of data were symmetrical. Mean values of PTH were 37.4 ± 17.9 pg/mL. PTH clearly increased by age in males and young females but slightly increased in elderly females. The elderly male group had the highest PTH values.

Age, body mass index, total calcium and PTH values of CAD patients and healthy controls are presented in Table 1. Coronary angiography was performed on all patients with CAD.

The mean age of CAD patients was more than that of the healthy controls. Mean PTH levels in patients with CAD were within the normal limit and not statistically different from the controls. We found that six CAD patients had PTH concentrations > 65 pg/mL without abnormal total calcium and phosphorus. Four patients had stable angina, and the remainders had unstable angina (1 single, 2

Table 1. Age, body mass index, total calcium, phosphorus and PTH values in controls and CAD patients.

	Controls (n= 103)	CAD Patients (n=109)	p Value
Age, year	59 ± 10	62 ± 10	0.423
Body mass index	24.3 ± 4.4	25.7 ± 3.7	NS
Total calcium, mg/dL	9.59 ± 0.83	9.64 ± 0.97	NS
Phosphorus, mg/dL	3.58 ± 0.65	3.46 ± 0.57	NS
PTH, pg/mL	37.4 ± 17.9	40.2 ± 21.8	NS

NS= not significant

Table 2. Comparison of age, body mass index, total calcium and PTH values in various numbers of coronary occlusion with normal coronary angiography patients.

	Normal CAG (n=13)	Single Vessel (n=22)	p Value	Double Vessel (n=28)	p Value	Triple Vessel (n=46)	p Value
Age	54 ± 9	60 ± 9	0.046	64 ± 9	0.001	63 ± 10	0.003
Body mass index	24.8 ± 3.8	25.7 ± 3.6	NS	25.8 ± 4.7	NS	25.6 ± 3.4	NS
Total calcium, mg/dL	9.7 ± 1.1	9.8 ± 0.9	NS	9.6 ± 0.7	NS	9.5 ± 1.1	NS
PTH, pg/mL	49.6 ± 25.0	43.7 ± 23.9	NS	38.8 ± 19.5	NS	40.2 ± 26.4	NS

NS= not significant

double and 3 triple vessel disease by coronary angiography). One stable angina patient had elevated PTH and total calcium. In addition, we divided the cases into four subgroups by coronary angiography results (normal coronary angiography, single, double and triple vessel disease) and compared the difference of the PTH levels as shown in Table 2. The mean age of the normal coronary angiography group was less than that of the other groups. There was no significant difference between this hormone level in the normal and the abnormal coronary groups.

DISCUSSION

Parathyroid hormone consists of 84 amino acids derived from a prohormone. It is involved in systemic calcium homeostasis. There are several techniques to detect circulating PTH. We chose the immunoassay that detects intact PTH only, and which does not detect the inactive hormone fragments, to avoid falsely high concentrations of PTH.

Although one dynamic study showed racial differences in intact PTH[7], mean values of intact PTH in our healthy controls did not significantly differ from reference values studied in the white population. Previous reports about intact PTH in healthy Thai volunteers by Chailurkit LO, et al has shown that PTH increased with advancing age in both men and women[8]. The same result was observed in many studies [9-11]. In our study, we find that distinctive event only in men. For women, PTH obviously changes in the young but slightly increases in the elderly. Partial PTH suppression may originate from high supplemental calcium intake in elderly Thai females at present[12,13].

This study of intact PTH in patients with coronary artery disease and healthy controls demonstrated that PTH levels of both groups were within the normal range. We did not find any difference of this hormone level between these two groups and among various numbers of coronary occlusion in CAD patients. Although the mean age of CAD patients was significantly higher than the controls, mean PTH concentration of CAD patients was not higher.

Watson KE, et al assessed the association between vascular calcification and serum levels of PTH in 173 subjects at high and moderate risk for coronary heart disease [14]. There was no correlation between extent of calcification and level of PTH. PTH was also not correlated with coronary calcification, or the ratio of coronary calcification to the extent of coronary stenosis measured by using an electron beam computed tomography in the study by Arad Y, et al[15].

However, PTH levels in patients with acute myocardial infarction (AMI) were reported to increase in some previous investigations. Ljunghall S, et al. reported PTH concentrations in 26 AMI patients. Serum PTH levels were significantly raised in AMI patients already on admission and did not normalize during the first three hospital days[16]. Kipshidze NN, et al studied men with ischemic heart disease. They demonstrated that the basal PTH level was increased in acute myocardial infarction, particularly during the subacute stage[17]. A prospective study by Herrmann G, et al has shown that PTH concentrations were elevated in about half of 56 patients exhibiting organic CAD, and PTH levels were highest in three vessels disease and in patients with evidence of myocardial infarction[18].

There was also an increase in serum PTH during the first day after onset of AMI in the study of plasma catecholamine, PTH and calcium by

Joborn H, et al. They suggested that endogenous epinephrine acted to lower the ionized calcium levels, thereby stimulating the secretion of PTH which would prevent a further decrease in plasma calcium[19].

About 5.5 per cent of our CAD patients had slightly elevated PTH levels without abnormal total calcium and phosphorus, while the same pattern was seen in about 6.8 per cent of healthy people. Primary hyperparathyroidism was likely to occur in about 1 per cent of patients with CAD if we considered the PTH and total calcium. A study carried out in 499 patients admitted to a coronary care unit by Joborn H, et al indicated that about 1.5 per cent of AMI patients had primary hyperparathyroidism [20].

Several problems limit interpretation of these data, especially PTH secretion. Pulsatile secretion of PTH may affect the results because PTH fluctuates at a frequency of 6-7 bursts per hour. Approximately 30 per cent of circulating PTH is attributable to pulsatile secretion[21]. Thus, further investigation must be done in larger populations to determine PTH status in CAD patients.

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การศึกษาเปรียบเทียบระดับฮอร์โมนพาราธัยรอยด์ในคนไทยที่เป็นโรคหลอดเลือดหัวใจกับผู้ที่มีสุขภาพแข็งแรง

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ระดับฮอร์โมนพาราธัยรอยด์มีผลต่อกระบวนการเมตะโบลิสม์ของแคลเซียม นอกจากนี้ยังมีผลต่อระบบหลอดเลือดและหัวใจ โดยมีเซลล์เป้าหมายคือเซลล์กล้ามเนื้อหัวใจและเซลล์กล้ามเนื้อเรียบ พบว่าผู้ป่วยโรคหัวใจหลายรายมีระดับฮอร์โมนพาราธัยรอยด์สูงกว่าปกติ วัตถุประสงค์ของการศึกษาครั้งนี้คือเพื่อเปรียบเทียบระดับฮอร์โมนพาราธัยรอยด์ในผู้ป่วยโรคหลอดเลือดหัวใจจำนวน 109 คน เทียบกับผู้ที่มีสุขภาพแข็งแรง 103 คน ค่าเฉลี่ยของระดับฮอร์โมนพาราธัยรอยด์ชนิดทั้งโมเลกุลในผู้ที่มีสุขภาพแข็งแรงและผู้ป่วยโรคหลอดเลือดหัวใจเท่ากับ 37.4 $\pm$ 17.9 และ 40.2 $\pm$ 21.8 ตามลำดับ ซึ่งไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ นอกจากนี้การเปรียบเทียบระดับฮอร์โมนพาราธัยรอยด์ในผู้ป่วยโรคหลอดเลือดหัวใจโดยแบ่งกลุ่มตามจำนวนหลอดเลือดหัวใจที่อุดตันก็ไม่พบความแตกต่างอย่างมีนัยสำคัญระหว่างกลุ่ม จากการศึกษาครั้งนี้ พอจะสรุปได้ว่าผู้ป่วยโรคหลอดเลือดหัวใจไม่ได้มีระดับฮอร์โมนพาราธัยรอยด์สูงกว่าคนทั่วไป

คำสำคัญ : โรคหลอดเลือดหัวใจ, ฮอร์โมนพาราธัยรอยด์

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