Calf and forearm blood flow in patients with primary hyperparathyroidism and in control subjects

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Abstract. Using a venous occlusion air-filled plethysmograph we measured the blood flow in the limbs in 10 patients with established primary hyperparathyroidism and control subjects. The patients had highly raised ionized calcium and immunoreactive parathormone levels, and the diagnosis was verified at operation. In all patients resting blood flow values in the limbs were increased compared with control subjects. Peak blood flow after 5 min of ischemia was also increased, however, not significantly. This clinical study supports previous studies on a vasoactive effect of parathormone.

Parathyroid hormone (PTH) may have hypotensive and vasodilator effects on various vascular beds in several animal species (1-4), and profound hypotension can be observed when administered to experimental animals (5). This is due to a decreased peripheral vascular resistance and increased flow in the renal, cardiac, hepatic, gastric and pancreatic circulation (2).

The purpose of the present work was to evaluate blood flow in the calf and forearm in patients with primary hyperparathyroidism at rest and during reactive hyperemia using plethysmography.

Patients and Methods

Ten women (mean age 47.4±17.7 years, range 25-60) suffering from primary hyperparathyroidism not complicated by peripheral obliterative vascular disease and 20 sex- and age-matched control subjects (mean age 43.8±10.2 years), without any clinical signs of peripheral obliterative vascular disease were selected for the study. The diagnosis of primary hyperparathyroidism was based on clinical and biochemical features and confirmed by operation and removal of a parathyroid adenoma composed primarily of chief cells. All patients had normal renal function determined by serum creatinine and none were taking any medication known to influence the cardiovascular system. Serum ionized calcium, phosphate, alkaline phosphatase, and C-terminal PTH were measured in the same serum specimen in each patient. Ionized calcium was measured in serum using a ion-selective electrode (Calcium analyzer 99-20 Orion Research Inc, Cambridge, MA) with a reproducibility of 0.5%. Serum immunoreactive PTH was determined using a PTH-RIA Kit (Sorin-Biomedica, Saluggia, Italy) with normal values 0.7±0.2 μg/l. The between-assay coefficient of variation is 10.6%. The system uses guinea-pig polyclonal antibodies directed toward the C-terminal sequence of synthetic human PTH (53-84).

For inclusion in the patient and control groups the patients should be free from discomfort in the extremities and the pulse should be present in the femoral and the popliteal artery, the dorsal artery of the foot, and the posterior tibial artery. None of the subjects had any systemic disease known to affect the circulation in the extremities and none was smoker. In all the patients the physical examination was completed with ECG, blood counts, and determination of blood cholesterol and lipids. All individuals gave informed consent to the study.

Measurements of blood flow in the calf and forearm in the patients and control subjects were made after the subjects had been lying down for at least 15 min, usually covered by a sheet or light blanket but with bare limbs. Room temperature varied from 22-26°C, but the temperature was constant during the individual period of recording. The resting blood flow after 15 min of bed rest and the peak blood flow after 5 min of ischemia were determined. The peripheral blood flow at the calf and
forearm level was measured using a venous occlusion air-filled plethysmograph (Fluvoscript forte, VEB Messgeräte Werke, Ballenstedt, GDR). This method has a coefficient of variation of 9.3% for resting blood flow and 6.6% for peak blood flow (6). The air-filled rubber cuff was placed on the thickest part of the calf and forearm. Venous occlusion is produced by means of a 15-cm wide cuff placed immediately above the patella and elbow and insufflated to a pressure of 50 mmHg. To produce 5 min of ischemia the occlusion cuff was insufflated to a pressure of about 250 mmHg. The first value following the emptying of the ischemia cuff is taken as the blood flow at 0 seconds, and values are measured after 15, 30, 45, 60, 120, 180, 240 and 300 s. The highest value was reported as peak blood flow (7). Blood flow are expressed as ml·min⁻¹·(100 ml tissue)⁻¹. The patients and control subjects had measurements made on both legs 2 times on different days to check the reproducibility of our measurements.

Systolic and diastolic blood pressure were measured simultaneously with blood flow using a mercury sphygomonanometer according to WHO criteria (8). We considered a systolic blood pressure >145 mmHg and diastolic blood pressure >95 mmHg arterial hypertension.

Statistical analysis was performed by means of the Student's t-test for unpaired data. Results are given as mean ± sd.

Table 1.

<table>
<thead>
<tr>
<th>Number</th>
<th>Controls</th>
<th>pHPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Blood pressure mmHg</td>
<td>43.8±10.2</td>
<td>47.4±17.7</td>
</tr>
<tr>
<td>Calf resting blood flow ml·min⁻¹·(100 ml)⁻¹</td>
<td>123/77</td>
<td>131/80</td>
</tr>
<tr>
<td>Calf peak blood flow ml·min⁻¹·(100 ml)⁻¹</td>
<td>2.94±1.10</td>
<td>4.50±2.56a</td>
</tr>
<tr>
<td>Forearm resting blood flow ml·min⁻¹·(100 ml)⁻¹</td>
<td>24.78±4.65</td>
<td>32.87±11.90</td>
</tr>
<tr>
<td>Forearm peak blood flow ml·min⁻¹·(100 ml)⁻¹</td>
<td>4.70±1.83</td>
<td>6.67±1.79a</td>
</tr>
<tr>
<td>Serum ionized calcium mmol/l</td>
<td>28.40±6.27</td>
<td>35.97±13.30</td>
</tr>
<tr>
<td>Serum PTH µg/l</td>
<td>1.21±0.10</td>
<td>1.79±0.21a</td>
</tr>
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</table>

(Mean ± sd) a: p<0.05

Results

Table 1 shows the results of peripheral blood flow measurements in the calf and forearm in the patients and control subjects. No patient had hypertension. Significant differences were found between the two groups with respect to serum ionized calcium and PTH.

The resting peripheral blood flow in both the calf and forearm was significantly increased in the patients (p<0.05). Calf and forearm peak blood flow were also increased in patients compared with controls, but this did not reach statistical significance. We did not find any correlation between peripheral blood flow and either PTH or ionized calcium values in our patients. There was a correlation between PTH and ionized calcium values (r=0.47, p<0.05).

Discussion

In 10 patients with primary hyperparathyroidism the blood flow in the limbs was measured, and the resting values were increased in all patients compared with age- and sex-matched controls. This may possibly be attributed to a reduction of the vascular resistance in the extremities. Peak blood flow was also increased, but did not reach statistical significance. It is probable that the decrease of the peripheral vascular resistance is already maximal and cannot be influenced further during reactive hyperemia. The control of vascular resistance is dependent on a complex interrelationship of endogenous and exogenous factors. Interpretation of the data obtained in this study is difficult, since primary hyperparathyroidism is a complex metabolic disorder not only characterized by hypercalcemia but also by hypophosphatemia and increased PTH levels. The lack of correlation between blood flow values and either serum PTH or ionized calcium may indicate that other factors (like duration of disease, local concentrations of ionized calcium and PTH, electrolytes) may modulate the tissue response to PTH. Furthermore, the measured PTH may include some biologically inactive fragments, suggesting that serum PTH determined by RIA does not always accurately reflect the peripheral action of the hormone (9).

Some evidence presented in the literature may allow speculation about the significance of the elevated concentrations of PTH and ionized calcium found in our study. PTH is an inhibitor of smooth
muscle construction in the cardiovascular system (10). Charbon et al. concluded that the hypotensive effect of PTH was due to a diminished peripheral resistance (11). Calcium plays a central role in the cellular events regulating contraction and relaxation in the vascular smooth muscle cells (12). Calcium can cause vasodilation, evident from a reddening and warming of the skin (13). Oral calcium loading has been found to be associated with a decline in blood pressure in humans (14,15).

The data presented demonstrated that resting blood flow in the limbs of our patients with primary hyperparathyroidism is increased in comparison with control subjects. Further experiments are needed to assess the precise physiological meaning of our findings and exact role of the increased concentration of ionized calcium and PTH.

References


Received September 24th, 1990.
Accepted January 11th, 1991.

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