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Parathyroid Function in Primary Osteoporosis

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ABSTRACT Two major species of serum immunoreactive parathyroid hormone (iPTH) were measured in 47 untreated patients with primary osteoporosis by using two highly specific radioimmunoassays. Mean iPTH was normal with one antiserum but was lower than normal (P < 0.001) with the other. iPTH values did not correlate with biochemical parameters or with the proportion of bone-resorbing surfaces in iliac crest bone biopsy specimens. These data suggest that the increased bone resorption is not due to increased parathyroid function in most osteoporotic patients. However, seven of our patients (15%) appear to represent a separate population because they had increased values with one or the other of the antisera.

INTRODUCTION

Because of morphometric (1, 2) and biochemical evidence (3) that bone resorption is increased in primary osteoporosis and because it is believed that bone resorption is primarily regulated by parathyroid hormone (PTH), PTH may play a causal or permissive role in the pathogenesis of osteoporosis (4-7). However, parathyroid function has not been assessed directly in this disorder.

We measured serum immunoreactive PTH concentrations (iPTH) in normal and in osteoporotic persons to determine if parathyroid function is abnormal in osteoporosis.

METHODS

We studied 47 ambulatory patients with progressive osteoporosis of sufficient severity to produce crush fractures of the spinal column. The 43 women and four men in the group had a mean age of 64.9 yr (range, 47-79 yr). No patient had any evident medical disease that might produce osteoporosis and none had any clinically evident condition that might impair calcium absorption, such as liver disease, previous subtotal gastrectomy, or sprue. All had normal serum values for calcium, phosphorus, and alkaline phosphatase. Formal studies of intestinal absorption were not made. iPTH was determined in these patients prior to the initiation of any form of treatment.

The patients remained on their habitual diets; blood for serum iPTH determinations was drawn at 8:00 a.m. after an overnight fast. On the same serum sample, calcium was determined by atomic absorption spectrophotometry and phosphorus and alkaline phosphatase, by standard methods. Bone-forming and bone-resorbing surfaces in an iliac crest biopsy sample were determined by quantitative microradiography (1) in 27 of these patients.

For control values, serum iPTH and calcium were also determined in 146 normals, none of whom had a history of back pain (84 women and 62 men with ages distributed evenly between 20 and 78 yr); these values include previously reported data from 52 normal persons (8). Bone densitometry values (9) of the radius, obtained for two-thirds of the normals more than 50 yr old, were within the normal range for their age.

iPTH was measured by radioimmunoassay using two different antisera (GP-1M and CH-14M). The first assay system used a guinea pig anti-porcine-PTH antiserum (GP-1M) and has been described in detail previously (8). It measures iPTH in greater than 95% of normal sera. Sera from all patients studied were assayed in this system. The second assay system used a chicken anti-bovine-PTH antiserum (CH-14M). This assay system measures iPTH in greater than 90% of normal sera. The radioimmunoassay was performed identically except that it was used at a higher concentration (1:3,000, compared with 1:100,000 for GP-1M) and that approximately five times less 125I-labeled bovine PTH was added to the incubation mixtures (3,000 cpm for CH-14M compared with 15,000 cpm for GP-1M). Incubation mixtures with CH-14M were counted for sufficient times to record 10,000 counts. Standard curves with CH-14M antiserum using both purified human PTH from hyperparathyroid serum and a standard preparation of human PTH obtained from the media of cultured parathyroid adenoma explants have been published previously (10, 11). Sera of 20 of the osteoporotic patients and 36 normals (17 more than 50 yr old) were assayed for iPTH using CH-14M antiserum. In both assays, the criteria for a measurable iPTH value were those previously published (8). Human hyperparathyroid serum was used as a refer-
ence standard in both assays and the coefficient of inter-
assay variation for replicate determinations was 12-14%.

Two major molecular species of PTH have been previ-
ously demonstrated in serum of patients with primary hyper-
parathyroidism (12, 13). The two antisera used in the pres-
ent study have markedly different specificities for these
two species. Gel-filtration studies of hyperparathyroid sera
have demonstrated that antiserum GP-1M predominantly
measures PTH immunoreactivity in fractions eluting in a
region corresponding to mol wt 7000 whereas antiserum
CH-14M predominantly measures immunoreactivity eluting
in the region of mol wt 9500. The normal range for iPTH
is undetectable to 40 μl-eq/ml measured with GP-1M and
undetectable to 250 μl-eq/ml with CH-14M. The difference
in the normal ranges obtained with these two antisera prob-
ably relates to (a) differences in the specificities of the
antisera for the 9500 and 7000 mol wt species of PTH in
hyperparathyroid serum and (b) apparent differences in the
concentration of these species in the standard hyperpar-
athyroid reference serum. From our studies, there appears
to be much less 9500 mol wt than 7000 mol wt species of
iPTH in hyperparathyroid serum. Therefore, since CH-14M
antisera is relatively specific for the 9500 mol wt species
of iPTH, it would require proportionally more standard
hyperparathyroid serum to achieve the same inhibition of
the immune reaction than with GP-1M.

RESULTS

iPTH values obtained with antiserum GP-1M. iPTH
was measurable in all but four sera from normals;

* Arnaud, C. D. Unpublished data.

VALUES did not differ significantly between men and
women. There was a small positive regression of
iPTH on age (r = 0.186, P < 0.05). As previously re-
ported (8), there was an inverse correlation of iPTH
with serum calcium concentration (r = -0.53, P
< 0.001). For 79 normals more than 50 yr old, mean
iPTH (±SE) was 22.4±0.9 μl-eq/ml.

For patients with osteoporosis, mean iPTH (±SE)
was 25.1±1.8 μl-eq/ml (range, 9.0-71.2), not signifi-
cantly different from that of normals more than 50 yr
old. The serum calcium values did not differ signifi-
cantly in the two groups. There was no significant cor-
relation of iPTH with serum calcium concentration
(Fig. 1) or with serum phosphorus or alkaline phos-
phatase or, in the 27 patients who had iliac crest biop-
sies, with the proportion of surfaces undergoing for-
mation or resorption.

Six of the 47 osteoporotic patients had iPTH values
that were above the 97.5 percentile limit for the re-
gression of iPTH on serum calcium concentration
in normals. Three of these six patients subsequently un-
derwent an intravenous infusion of calcium (as the
D-glucosamine, 4 mg/kg per h for 4 h in two and 8 h
in one); at this time all three were receiving treat-
ment for their osteoporosis (calcium supplements and
calcitonin for 6 months in two and phosphate supple-
ments for 3 months in one). iPTH remained un-
changed or increased slightly during the 8 h after the
beginning of the infusion to two patients; it decreased
from 71 to 11 μl-eq/ml in one (Fig. 2). In four normals
who received a 4 h infusion of calcium at the same
rate, iPTH was undetectable by 2 h and remained so
through 12 h (8).

iPTH values obtained with antiserum CH-14M.
iPTH was measurable in all but two sera from nor-
mals; values did not differ significantly between men
and women or between individuals over and under age

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**FIGURE 1** Serum iPTH (antiserum GP-1M) as function
of serum calcium. Individual values for normals over age
50 yr are given by (○); regression line and 95% confi-
dence limits are given by broken lines. Individual values
for osteoporotic patients are given by (●). Patients desig-
nated by numbers 1, 2, and 3 underwent intravenous calcium
infusions; iPTH was not suppressed in patients 1 and 2
but was suppressed in patient 3. Patient 4 had high iPTH
values with antiserum CH-14M.

**FIGURE 2** iPTH values in three patients who received
intravenous calcium infusions (4 mg/kg per h for 4 h
in patients 1 and 2 and for 8 h in patient 3). Designation
of patients is as in Fig. 1.
of osteoporotic patients-a form of iPTH (assayed with antiserum CH-14M) which was not the same as in Fig. 1. Patients 1, 2, and 3 were the only patients reassayed with antiserum CH-14M who had higher than normal iPTH values with antiserum GP-1M.

patients with increased iPTH values (six with antiserum GP-1M and one with antiserum CH-14M), five had serum calcium concentrations in the high normal range and it is possible that they represent examples of normocalcemic primary hyperparathyroidism. This possibility is particularly likely in the two patients whose iPTH values were not suppressed by intravenous calcium infusion, although prior treatment may have influenced these results. That more patients had increased values for iPTH with antiserum GP-1M than with CH-14M is consistent with the greater ability of the former antiserum to separate normals from those with primary hyperparathyroidism (16). An alternative possibility is that increased iPTH in these seven patients was due to secondary hyperparathyroidism resulting from occult intestinal malabsorption of calcium.

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REFERENCES


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