Rapid Intravenous Calcium Infusion Test in Sarcoidosis*


Previous reports have described a distinctive pattern of phosphorus excretion (after rapid calcium infusion) in sarcoidosis. The author performed similar studies on eight patients with sarcoidosis and five patients with other pathologic processes. A “sarcoid pattern” was noted in only one patient with sarcoidosis and in two patients with tuberculosis. It can be stated that the rapid calcium infusion test is not a diagnostic aid in sarcoidosis.

Abnormalities of calcium metabolism, hypercalcemia and hypercalciuria have been well documented in association with sarcoidosis.1,2 During their formulation of a rapid calcium infusion study for the diagnosis of hyperparathyroidism, Goldsmith and his associates3,4 demonstrated a distinctive pattern of phosphorus excretion (UP/UCr) in patients with sarcoidosis. It is our intent in this communication to present additional observations on this procedure both in sarcoidosis and other disorders.

METHODS

The intravenous calcium infusion study was performed according to the method of Goldsmith and colleagues.5,4 Each patient was provided a low calcium (less than 250 mg) and low phosphorus (less than 700 mg) diet for a period of five to seven days prior to the test. Following an overnight fast, a loading dose of 250 ml of distilled water was administered orally at 7 AM and at hourly intervals thereafter until the completion of the study. At 8 AM, the patient voided and the specimen was discarded. Subsequently, at hourly intervals, urine specimens were collected for creatinine and phosphorus determinations until 12 AM. At 9 AM, 180 mg of calcium glucoheptonate was infused intravenously over a ten-minute period. The initial urine specimen at 9 AM, was designated "C", and the subsequent specimens at 10 AM, 11 AM, and 12 AM were respectively labeled "1", "2", "3." The creatinine excretion for all time intervals was evaluated for comparability.

Urinary creatinine and phosphorus determinations were performed according to the methods of Folin and Wu,5 and Fiske and Subbarow.6 Calcium determinations were performed according to the method of Kessler and Wolfman.7 The urinary phosphorus excretion was expressed as the ratio of the urinary phosphorus concentration to the urinary creatinine concentration (UP/UCr). Subsequent to a calcium infusion in normal subjects, Goldsmith and his associates noted that the values for phosphorus excretion in collection period "2" were always less than those of the initial specimen "C." In contrast, patients with hyperparathyroidism had values for phosphorus excretion in collection period "2" that were greater than those of both specimen "C" and specimen "1." An intermediate response in phosphorus excretion was elicited in patients with sarcoidosis. Although phosphorus excretion in period "2" was greater than in period "C," it was less than "1."

RESULTS

Eight patients with sarcoidosis were investigated. The vital statistics and results of the calcium infusion studies are presented in Table 1. The diagnosis of sarcoidosis was confirmed in all instances with an open lung biopsy. Special stains and cultures of secretions and biopsy specimens were negative for both mycobacteria and fungi. No patient had either hypercalcemia or hypercalciuria. Corticosteroid therapy had not been administered to any patient. All patients with a single exception had a normal pattern of phosphorus excretion following the calcium infusion. The single exception (FP) had a “sarcoid” pattern with the phosphorus excretion in period “2” greater than...
RAPID IV CALCIUM TEST IN SARCOIDOSIS

SARCOID

Figure 1. Mean values with standard deviations in UP/UCr following calcium infusion in sarcoidosis.

The intravenous calcium infusion study was also evaluated in an additional five patients with a variety of disorders. The vital statistics, diagnoses and results of the phosphorus excretion in these patients are presented in Table 2. As in the patients with sarcoidosis, none had evidence of hypercalcemia or hypercalciuria, or had received corticosteroids. Three of the patients had normal responses to the calcium infusion as determined by the patterns of their phosphorus excretion. However, both a patient with lymphohematogenous tuberculosis and a patient with pulmonary tuberculosis had a "sarcoid" pattern. The diagnosis of tuberculosis in both instances was substantiated by positive cultures for Mycobacterium tuberculosis.

**Comments**

The singularity of the abnormalities in calcium metabolism in sarcoidosis represents a fertile field of investigation for the development of a simplified diagnostic procedure that will distinguish this entity from the pathologic processes that may mimic it. It was with this aspiration that the current investigation was undertaken. Goldsmith and his associates in the evaluation of a rapid calcium infusion study for the diagnosis of hyperparathyroidism noted a distinctive pattern of phosphorus excretion in patients with sarcoidosis. The presence of hypercalcemia, hypercalciuria or radiographic evidence of bone involvement was not commented upon.

Utilizing a different method of calcium infusion, Roos evaluated 14 patients with a histologic diagnosis of sarcoidosis. Twelve of these patients manifested an abnormal pattern of urinary phosphorus excretion. This was corrected in 11 by the concurrent administration of either vitamin D, corticosteroids, or adrenocorticotropic hormone (ACTH). Cessation of therapy resulted in a reversion of the urinary phosphorus excretion to its previously abnormal pattern. There was no correlation with the serum calcium level, which was elevated in three of the patients. However, radiographic evidence of bone involvement was detected in 8 of the 12 patients with an abnormal urinary phosphorus excretion. Roos postulated that the abnormality in urinary phosphorus excretion reflected a compensatory increase in function of the parathyroids, secondary to sarcoid involvement of bone. This was reflected in a rise in the serum phosphorus level with the intravenous administration of calcium and a pattern of urinary phosphorus excretion that resembled that found in patients with sarcoidosis.

**Table 2—Miscellaneous, Vital Statistics, Diagnosis and Laboratory Data**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Phosphorus Excretion (UP/UCr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>41</td>
<td>M</td>
<td>Pulmonary histoplasmosis</td>
<td>.18  .37  .34  .29</td>
</tr>
<tr>
<td>10</td>
<td>21</td>
<td>M</td>
<td>Hodgkin's disease</td>
<td>.40  .32  .29  .65</td>
</tr>
<tr>
<td>11</td>
<td>24</td>
<td>M</td>
<td>Sarcoidosis and pneumoconiosis</td>
<td>.51  .43  .46  .42</td>
</tr>
<tr>
<td>12</td>
<td>47</td>
<td>F</td>
<td>Lymphohematogenous tuberculosis</td>
<td>.21  .31  .26  .29</td>
</tr>
<tr>
<td>13</td>
<td>36</td>
<td>M</td>
<td>Pulmonary tuberculosis</td>
<td>.12  .19  .16  .40</td>
</tr>
</tbody>
</table>

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tients with hyperparathyroidism.

In the present study, the characteristic pattern of urinary phosphorus excretion following the rapid intravenous administration of calcium was noted in only one of eight patients investigated. However, it was also found in two patients with tuberculosis, pulmonary and lymphohematogenous. None of the subjects of this investigation had either hypercalcemia, hypercalciuria, or radiographic evidence of bone disease. In no instance did the pattern of urinary phosphorus excretion resemble that found in hyperparathyroidism.

The disparities that exist between the present study and those of Goldsmith and Roos are difficult to reconcile, since the etiology of hypercalcemia in sarcoidosis remains undefined. The most acceptable hypothesis at present is a hypersensitivity to vitamin D. The findings of hypercalcemia, hypercalciuria, and a decreased fecal calcium are common to both sarcoidosis and vitamin D intoxication. The administration of vitamin D has induced these changes in sarcoidosis. Although corticosteroids correct the biochemical abnormalities in both entities, the abnormalities in bone metabolism in sarcoidosis persist. The majority of patients with sarcoidosis and hypercalcemia have histologically normal glands. However, certain patients with sarcoidosis demonstrate an exaggerated response to the administration of parathyroid extract, which can be altered by the concurrent administration of corticosteroids. This finding provides substance to the hypothesis of Roos that the abnormalities in urinary phosphorus excretion in sarcoidosis are secondary to an augmentation in parathyroid function.

The pattern in urinary phosphorus excretion following the rapid intravenous administration of calcium is not sufficiently specific to serve as a diagnostic study in sarcoidosis. However, it has merit as an investigative procedure providing further insight into the etiology of the hypercalcemia of sarcoidosis.

REFERENCES


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The Dawn of Scientific Biology

In 1828 Fiedrich Woehler (1800-1882) ended all doubts about whether laboratory methods could duplicate the intricate substances elaborated by living plants and animals. He synthesized urea, and knowledge of this compound proved the key to understanding a host of others. In 1838 M. Schleiden (1804-1881) drew together all previous evidence, added some of his own and convinced botanists that the ultimate unit of plant life was the cell. Next year his friend Theodor Schwann (1810-1882) proved the same theory for animal life and thus gave biology sound working units comparable to Dalton's atoms in chemistry.

Stevers, M: Mind Through the Ages. New York, Doubleday, 1940