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# Hypercalcemia in Pulmonary Tuberculosis

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## ABSTRACT

Tuberculosis can affect calcium metabolism, mainly through an enhanced production of active vitamin D. The incidence of hypercalcemia among unselected patients with active pulmonary tuberculosis was investigated, retrospectively, during a ten-year period. Among 67 patients, the mean serum calcium concentration on admission was significantly raised compared to healthy controls (2.51 ± 0.16 (SD) vs 2.43 ± 0.07 mmol/l; $p<0.001$) and 25 % of the patients had hypercalcemia. After one year of successful tuberculostatic treatment the serum calcium values had normalized.

## INTRODUCTION

Active pulmonary tuberculosis can be accompanied by disturbances of calcium metabolism (1, 3, 4, 6, 9, 10). Sevral mechanisms could be involved, e.g. increased production of bone-resorbing factors (8), a reduced degradation of prostaglandins (1), but an enhanced synthesis of active vitamin D is generally considered to be most important (3, 5, 6, 7, 9), as also established in sarcoidosis (2, 5, 11).

In clinical practice hypercalcemia is not recognized as a common complication of tuberculosis but there is little information about its incidence among unselected patients.

## MATERIAL AND METHODS

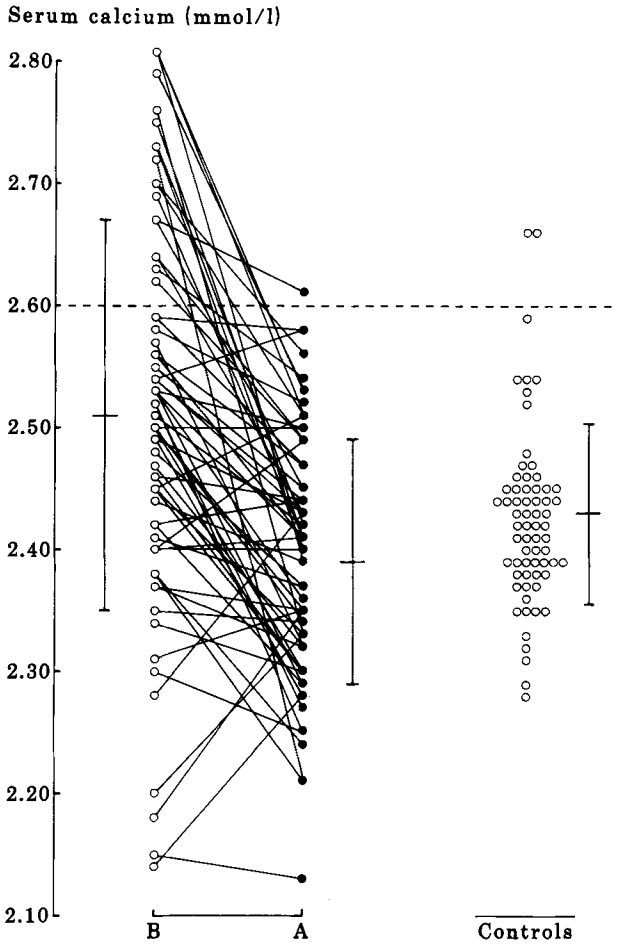
Hospital records from patients being treated for pulmonary tuberculosis at the Departments of Lung Diseases at Gävle County Hospital, Sweden, during the years 1976 through 1985, were investigated in retrospect. All of the following criteria were fulfilled by each patient:

1. Pulmonary tuberculosis visible at chest X-ray and verified by positive direct sputum examination or positive Loewenstein culture.
2. Uninterrupted and uncomplicated treatment for one year with isoniazid and rifampicin, supplemented with myambutol for the first three months.
3. Healing of the disease after one year as could be judged from chest X-ray, laboratory and clinical findings.

4. Pretreatment and post-treatment (at 11-12 months) values of serum calcium and albumin measured in the same autoanalyzer.
5. The patient should not have received vitamin D or calcium supplementation either before or during chemotherapy.

Sixty-seven patients (mean age 60 ± 14 years, 39 men and 28 women) fulfilled the criteria. For comparison of serum calcium values a control group, recruited from a health survey, was investigated. Serum calcium and albumin were measured in the autoanalyzer (SMAC, Technicon, USA) used in hospital practice. The values of serum calcium, with a reference range of 2.20-2.60 mmol/l, are all adjusted for albumin. The coefficient of variation for serum calcium is 1-2 %.

Treatment effects as well as the comparison between patients and the controls were statistically analysed by Student's t-test. Comparisons of the proportions of hypercalcemia in patients and controls were made by the chi-square test.



## RESULTS

Among the 67 patients with pulmonary tuberculosis 25 % were hypercalcemic (more than 2.60 mmol/l) before initiation of chemotherapy. Only two persons (3 %) showed hypercalcemia in the control group ($p<0.001$).

The mean value for serum calcium in the patients before treatment was 2.51 ± 0.16 (SD) mmol/l which was significantly higher than the mean level found in the control population (2.43 ± 0.07, $p<0.001$).

After one month of treatment serum calcium levels had decreased to 2.45 ± 0.11 ($p<0.05$) and a further reduction to 2.39 ± 0.10 mmol/l was seen at the end of chemotherapy ($p<0.01$, see figure). At this time only one patient had a serum calcium value above the reference range. All together 52 of the 67 patients (78 %) displayed a reduction of the serum calcium values during treatment.

The changes of serum calcium were also evident when the values were adjusted for the small rise (2 g/l) in serum albumin which occurred during therapy.

## DISCUSSION

Our study demonstrates that mild hypercalcemia is a common finding in unselected patients with pulmonary tuberculosis. While other reports found hypercalcemia generally associated with vitamin D supplementation and sunlight exposure, all our patients with high serum calcium levels were hypercalcemic without supplementation. The uniform distribution of calcium levels before treatment suggests that the alterations of calcium metabolism are not restricted to a few hypercalcemic subjects but is a general phenomenon which accompanies pulmonary tuberculosis. Serum calcium also decreased uniformly in most patients after prolonged chemotherapy.

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