原　著

CALCIUM HOMEOSTASIS IN UNTREATED PULMONARY TUBERCULOSIS II－DYNAMIC STUDY

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Oral calcium tolerance test was done for 17 normal subjects and 26 pulmonary tuberculous patients. Ingestion of 1 gm calcium did not alter serum calcium levels significantly, while urinary calcium significantly increased in normal controls ($p<0.001$) and significantly decreased in tuberculous patients.

The decrease in urinary calcium in untreated TB patients may be attributed to the associated decrease in serum concentration of 25-hydroxyvitamin D. Serum PTH and nephrogenous cAMP showed insignificant changes both in controls and TB patients. Meanwhile, these changes are antiparallel to serum calcium, denoting a normal response (function) of parathyroid gland to serum calcium alterations.

Key words : Calcium tolerance test, Tuberculosis, Cyclic AMP, Parathyroid hormone.

INTRODUCTION

The incidence of hypercalcaemia associated with active tuberculosis is a documented finding (1, 2).

Ojwang et al. (3) suggested that PTH, or substances with similar biological activity on bone, may particapate in causation of hypercalcaemia. Shai et al. (4) suggested that calcium deficiency present prior to admission causes a degree of hyperparathyroidism comparable to that which occurs in renal disease, and excess secretion of parathyroid hormone persists after the deficiency is corrected. Evaluation of parathyroid hormone in the serum of patients with active pulmonary tuberculosis was attempted in a study by Gomaa (2) and a significant rise in serum parathyroid hormone was observed.

Oral calcium tolerance test was advocated by Broadus et al. (5), Broadus and Rasmussen (6) as a diagnostic and investigational aid in hyperparathyroidism. This test measures parathyroid function through simultaneous measurement of renal handling of calcium, phosphorus

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and cAMP and the response of these variables to an oral calcium load.

This study is a trial to evaluate the parathyroid function in patients with active pulmonary tuberculosis using oral calcium tolerance test.

MATERIAL AND METHODS

Fourty-three subjects constituted the material of this work. They were selected from the same subjects included in our previous study (7) :

1. Health control (Group Ⅰ, n=17) aged 20-56 y.
2. Tuberculous patients (Group Ⅱ, n=26) aged 18-28 y.

They were subcalssified according to National Tuberculosis Association of the USA (8) into : Group Ⅱa (n=11) with moderately advanced lesions and Group Ⅱb (n=15) with far-advanced lesions.

All patients and normal control subjects were subjected to an identical study protocol for oral calcium tolerance test (9).

Serum and urine samples were collected from each subject. Calcium (10) and creatinine (11) were measured by direct colourimetric determination.

PTH (12) and cyclic AMP (13) were measured by radioimmunoassay.

Urinary and nephrogenous cAMP were expressed as a function of glomerular filteration rate according to Broadus et al. (14).

The obtained data were statistically analysed by Student's "t" test for paired and unpaired data.

RESULTS

The results are presented in tables 1 & 2.

DISCUSSION

The decrease in serum calcium in tuberculous patients may be due to a large amount of oral calcium that might be lost in faeces as a result of impaired intestinal absorption of calcium in patients with active pulmonary tuberculosis as reported by Singhellakis et al. (15). Haemodilution may be a contributing factor in tuberculous patients. This haemodilution might be masked by increased intestinal calcium absorption in the normal control group, so that the mean difference in serum calcium appeared insignificantly increased.

Similar results were obtainted by Broadus et al. (5), (14), (16) and by Madvig et al. (9) concerning the normal control group.

The reported decrease in intestinal calcium absorption in patients with active pulmonary tuberculosis may be attributed to decreased serum concentrations of 25-hydroxycholeciferol

Table 1. Changes in Serum and Urinary Calcium in Normal Control (Group Ⅰ) and Tuberculous Patients (Group Ⅱ a, b) during Oral Calcium Tolerance Test.

Group	Parameter	Serum Calcium (mg/dl)			Urinary Calcium (mg/dl) §		
		Before	After	d'	Before	After	d'
Group Ⅰ n = 17	Mean	10.17	10.36	0.19	0.34	0.40	0.06
	SE			0.286			0.013
	P			> 0.05			< 0.001
Group Ⅱa n = 11	Mean	8.29	7.63	− 0.664	0.27	0.26	− 0.01
	SE			0.554			0.013
	P			> 0.05			> 0.05
	P_1			> 0.05			< 0.001
Group Ⅱb	Mean	8.71	8.16	− 0.546	0.34	0.32	− 0.02
	SE			0.232			0.016
	P			> 0.05			> 0.05
	P_1			> 0.05			< 0.001
	P_2			> 0.05			> 0.05

Table 2. Changes in Serum PTH and Nephrogenous cAMP (NcAMP) in Normal Control (Group I) and Tuberculous Patients (Group II a, b) during Oral Calcium Tolerance Test.

Group	Parameter	Serum PTH (pg/ml)			NcAMP (pmol/dl) §		
		Before	After	d′	Before	After	d′
Group I n = 17	Mean	130.60	125.25	− 5.35	3.70	3.26	− 0.44
	SE			3.300			0.414
	P			> 0.05			> 0.05
Group IIa n = 11	Mean	118.30	122.66	4.36	4.56	4.69	0.13
	SE			5.057			0.351
	P			> 0.05			> 0.05
	P_1			> 0.05			> 0.05
Group IIb	Mean	88.73	94.86	6.13	5.05	5.23	0.18
	SE			11.010			0.219
	P			> 0.05			> 0.05
	P_1			> 0.05			> 0.05
	P_2			> 0.05			> 0.05

P : Comparison between Before and After Within the Same Group (Paired "t").
P_1 : Results Compared to the Normal Control Group (Group I).
P_2 : Results Compared to The Tuberculous Group With Moderately Advanced Lesions (Group II a)
d′ : The Mean Difference between The estimated Values during Oral Calcium Tolerance Test.
§ : Related to Glomerular Filtrate.

(16), which is the precursor of 1,25-dihydroxycholecalciferol.

Urinary calcium excretion was significantly increased in the normal control subjects but declined significantly in tuberculous groups (groups IIa & b ; $p<0.001$). On the contrary, the changes in urinary calcium excretion after oral calcium was virtually identical in both groups of tuberculous patients. Although the mean decrease in urinary calcium exretion was more marked in cases with far-advanced lesions compared to that with moderately advanced lesions, the difference was statistically insignificant ($p<0.05$).

The increase in urinary calcium after calcium intake in normal subjects is in agreement with Madvig et al. (9).

Broadus et al. (5) reported a strongly positive correlation between the values of serum 1,25-dihydroxyvitamin D_3 and the calciuric response in patients with hyperparathyroidism, whereas Madvig et al. (9) stated that the difference in vitamin D status may influence the calciuric response. Based on these findings we can explain that the discrepancy between the calciuric response in normal controls and that in tuberculous groups may be attributed to decreased serum concentrations of 25-hydroxyvitamin D_3 in patients with untreated tuberculosis as reported by Davies et al. (17).

Both the reduction in serum PTH in normal controls and its increase in the tuberculous groups following oral calcium are anti-parallel to changes in serum calcium in the same groups, denoting a normal response of parathyroid gland to alterations in serum calcuim in tuberculous patients, became the parathyroid gland responds to the hypocalcaemia by increased production of PTH.

The use of urinary cAMP excretion as an index of PTH action is based on the fact that PTH stimulates cAMP synthesis in the renal cortex. Total urinary cAMP is derived from both the nephrogenous pool and plasma filtrate

(18).

Urinary cAMP was expressed in nanomoles/dl glomerular filtrate to avoid the effect of moderate renal failure, or to exclude patients who were considered to be under "stress" in whome plasma cAMP was moderately elevated with a coincident "apparent" lowering of NcAMP as expressed by the clearance ratio. The expression nanomoles per 100 ml glomerular filtrate provides an accurate quantitation of nephrogenous cAMP under all circumstances (14).

In this study, after the ingestion of 1 g calcium, nephrogenous cAMP was insignificantly altered in the normal control group, and TB subgroups.

The suppression of cAMP following oral calcium intake in normal controls is in agreement with Broadus et al. (14) and Madvig et al. (9).

Broadus (19) stated that the effects of PTH appears to account for 90–100% of the nephrogenous component of cAMP excretion. Based on this statement the suppression of NcAMP in normal controls and its increase in the tuberculous groups following oral calcium are parallel to changes in serum PTH in the same groups, denoting a normal response to the increase in serum parathyroid hormone in the tuberculous groups.

From the previous results we can conclude that the parathyroid gland response in active pulmonary tuberculosis is normal. The hypercalcaemia that may occur during treatment of active pulmonary tuberculosis and reported by several investigators cannot be due to hyperparathyroidism and may rather be due to other factors such as the effect of antituberculous drugs or increased sensitivity to vitamin D. Thus it is recommended to measure vitamin D metabolites in tuberculosis

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