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Calcium Metabolism in Normal and in Hypercalciuric Patients on Farnolith®, a Dietary Fibre Preparation

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Summary. In the present study Farnolith® (a granular powder consisting of different dietary fibres) was given to normals ($n = 6$), patients suffering from absorptive hypercalciuria type I ($n = 6$) and to one patient suffering from renal hypercalciuria. Farnolith binds calcium and reduces the calcium absorption from the intestine. In normals the urine- and serum parameters of calcium metabolism (total- and ionised calcium, parathyroid hormone and vitamin-D-metabolites) remained unchanged. In patients suffering from absorptive hypercalciuria type I a significant reduction of hypercalciuria was found; oxalic acid excretion had decreased as well. Lowered parathyroid hormone values returned to normal, vitamin-D-metabolites remained unaffected. In one patient suffering from renal hypercalciuria parathyroid hormone and 1,25-dihydroxy-vitamin D values increased, calcium excretion had not decreased, though. Our investigation shows that Farnolith® is suitable for the treatment of absorptive hypercalciuria. Calcium homoeostasis is returned to normal by Farnolith®, at the same time it does not produce secondary hyperoxaluria (as e.g. sodium cellulose phosphate). Patients with primary renal calcium loss should not be treated by Farnolith.

Key words: Hypercalciuria – Dietary fibres – Parathyroid hormon – 1,25-dihydroxyvitamin D

Introduction

According to Pak [8], patients suffering from absorptive hypercalciuria type I should be treated by calcium binders as e.g. sodium cellulose phosphate. These substances bind calcium and reduce the intestinal calcium absorption. The essential disadvantage of this substance, is that it produces an increase of oxalic acid absorption and hyperoxaluria.

Investigations conducted by James [4], Harmuth-Hoene [2] and Griffith [1] have shwon that calcium uptake from the interstine can be reduced by increased uptake of dietary fibre. By giving rice- or wheat bran to urinary stone patients, a significant reduction of calcium excretion was achieved [5, 7].

Farnolith® is a dietary fibre currently undergoing trial in the FRG. Due to its high cellulose composition it produces – unlike sodium cellulose phosphate a reduced oxalate and phosphate resorption. Preliminary results have shown that Farnolith® brings about a reduction of calcium excretion and an increase in citrate secretion [3].

Calcium binding substances, may affect calcium metabolism. Insufficient absorption of calcium from the intestine may arise causing an increased mobilisation of calcium from the bone with the eventual production of osteoporosis.

That is why we conducted investigations on calcium metabolism under Farnolith® – therapy in normals and in hypercalciuric patients.

Materials and Methods

Farnolith® is a granular powder consisting of different dietary fibres as e.g. wheat-, malt- and soy bran or guar-flour (Table 1). Wheat bran mostly consists of cellulose and hemicellulose, by which intestinal calcium absorption is reduced [2]. Soy bran is composed mainly of hemicelluloses and plant rubber, which is capable of swelling and reduces the absorption of bile acid in the intestine. In this way the absorption of oxalic acid can be reduced. Calcium tartrate increases the citrate excretion in the urine. Moreover Farnolith® contains the daily requirements of magnesium (300 mg).

6 normals (3 male, 3 female) and 6 patients (4 male, 2 female) with absorptive hypercalciuria type I (according to Pak (8) were treated with Farnolith® (normals for 3 months, patients for 18 months). Moreover one patient (male) with renal hypercalciuria, who tolerated thiazide medication badly, was treated with Farnolith® for 3 months. Dosage was 15 g twice a day before meals. Patients were given low calcium diet, normals mainfained a normal diet. The test subjects were advised to drink at least two liters a day.

Blood was taken and 24-hour urine collected at the outset, after one week (normals only), after 1, 3, 6, and 18 months.

The following blood parameters were evaluated: total calcium and ionised calcium, phosphate, magnesium, parathyroid hormone, calcitonin, 1,25-dihydroxycholecalciferol, 25-hydroxycholecalciferol.

Table 1. Composition of the dietary fibre Farnolith®

100 g of Farnolith® contain	
88.000 g	dietary fibres of wheat-, malt- and soy-bran (in proportion of 1 to 1 to 1)
3.200 g	Guar flour
4.500 g	potassium as dipotassium tartrate
1.300 g	magnesium as magnesium oxide
0.060 g	ferrum as ferrous fumarate
0.033 g	zinc oxide

Table 2. Determination methods of blood- and urine parameters tested

Serum	24-hour urin
Total Calcium (Nova 7)	Calcium (atomic absorpt.)
Ion. Calcium (Nova 7)	Magnesium (atomic absorpt.)
Phosphate (Boehringer)	Phosphate (Boehringer)
Magnesium (Atomabsorpt.)	Citrate (Boehringer)
Parathyroid hormone (RIA, C. Term)	Oxalic acid (Sigma)
Calcitonin (RIA)	
1,25-Vitp. D (CPBA)	
25-Vit. D (CPBA)	

Table 3. Blood- and urine parameters in $n = 6$ normals before and on Farnolith® administration ($\bar{x} \pm s$)

			before Farnolith®-therapy	on Farnolith®-therapy		
				1 week	1 month	3 months
blood	Ca	mmol/l	2.45 ± 0.06	2.29 ± 0.12	2.29 ± 0.07	2.28 ± 0.05
	Ca^{2+}	mmol/l	1.25 ± 0.05	1.22 ± 0.05	1.27 ± 0.05	1.25 ± 0.03
	PHT	ng/ml	0.11 ± 0.02	0.11 ± 0.05	0.13 ± 0.07	0.13 ± 0.06
	1,25 DHCC	pg/ml	62.4 ± 10.4	62.1 ± 11.1	57.2 ± 8.80	69.8 ± 21.1
	P_i	mmol/l	1.22 ± 0.16	1.28 ± 0.31	1.26 ± 0.07	1.21 ± 0.08
	Mg	mmol/l	0.81 ± 0.05	0.78 ± 0.13	0.84 ± 0.06	0.80 ± 0.05
urine	Ca	mmol/24 h	7.93 ± 2.72	5.62 ± 2.17	5.72 ± 1.93	5.84 ± 1.91
	Mg	mmol/24 h	7.03 ± 1.95	7.31 ± 1.56	6.41 ± 1.61	7.01 ± 1.72
	P_i	mmol/24 h	34.3 ± 7.20	36.1 ± 5.50	32.6 ± 6.10	33.4 ± 6.30
	Ox. ac.	mmol/24 h	0.33 ± 0.14	0.29 ± 0.11	0.30 ± 0.13	0.28 ± 0.14
	Citr.	mmol/24 h	2.99 ± 0.84	3.59 ± 0.79	3.51 ± 0.43	3.43 ± 0.97

Table 4. Blood- and urine parameters in $n = 6$ patients suffering from absorptive hypercalciuria type I before and on Farnolith® administration ($\bar{x} \pm s$)

		before Farnolith®-therapy	on Farnolith®-therapy				
			1 month	3 months	6 months	12 months	18 months
blood							
Ca	mmol/l	2.36 ± 0.15	2.32 ± 0.08	2.32 ± 0.09	2.38 ± 0.06	2.39 ± 0.07	2.28 ± 0.06
Ca^{2+}	mmol/l	1.15 ± 0.52	1.22 ± 0.38	1.22 ± 0.03	1.24 ± 0.04	1.22 ± 0.05	1.17 ± 0.05
PTH	ng/ml	0.18 ± 0.17	0.25 ± 0.15	0.26 ± 0.19	0.33 ± 0.23	0.41 ± 0.14*	0.42 ± 0.17*
1,25 DHCC	pg/ml	62.7 ± 18.8	50.3 ± 16.7	53.2 ± 17.4	60.7 ± 19.1	55.2 ± 15.4	57.1 ± 16.5
P_i	mmol/l	1.04 ± 0.09	0.99 ± 0.19	1.01 ± 0.14	1.06 ± 0.08	1.05 ± 0.07	1.01 ± 0.06
Mg	mmol/l	0.88 ± 0.19	0.83 ± 0.08	0.83 ± 0.05	0.83 ± 0.05	0.79 ± 0.06	0.86 ± 0.03
urine							
Ca	mmol/24 h	9.65 ± 1.22	5.65 ± 1.08**	6.64 ± 1.29**	5.97 ± 1.21**	5.66 ± 1.48**	6.24 ± 0.36**
Mg	mmol/24 h	5.26 ± 2.00	6.02 ± 1.70	4.98 ± 1.99	6.14 ± 2.00	4.85 ± 2.14	4.92 ± 0.91
P_i	mmol/24 h	31.3 ± 5.8	31.3 ± 3.9	28.3 ± 9.2	27.3 ± 5.1	23.3 ± 6.5	30.6 ± 13.1
Ox. ac.	mmol/24 h	0.59 ± 0.30	0.20 ± 0.12**	0.20 ± 0.11**	0.25 ± 0.08**	0.26 ± 0.11**	0.21 ± 0.10**
Citr.	mmol/24 h	2.35 ± 0.58	2.98 ± 0.88	2.87 ± 1.29	2.87 ± 1.29	2.93 ± 1.07	2.92 ± 0.53

* $p \leq 0.05$; ** $p \leq 0.01$

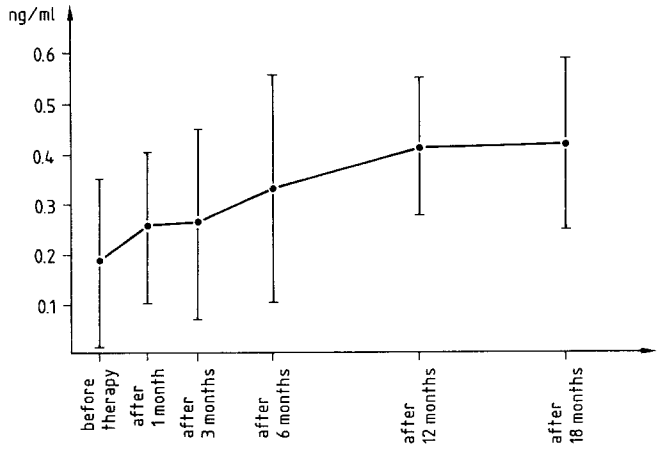

Fig. 1. Parathyroid hormone in the serum of $n = 6$ patients suffering from absorptive hypercalciuria type I before and on Farnolith® administration ($\bar{x} \pm s$)

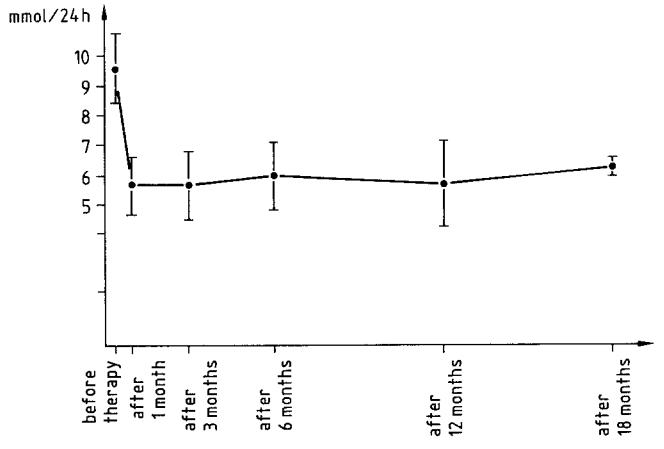

Fig. 2. Calcium excretion in the urine in $n = 6$ patients suffering from absorptive hypercalciuria type I before and on Farnolith® administration ($\bar{x} \pm s$)

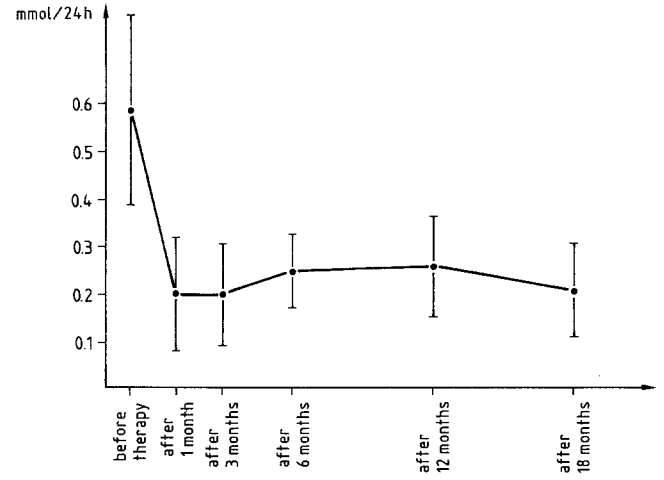

Fig. 3. Oxalic acid excretion in the urine in $n = 6$ patients suffering from absorptive hypercalciuria type I before and on Farnolith® administration ($\bar{x} \pm s$)

Calcium, phosphate, magnesium citrate and oxalic acid were determined in 24-hour urine collections. Methods of determination are presented in Table 2. Statistic evaluation was done by Mann-Whitney-tests.

Results

Total- and ionised calcium concentration in serum did not change in *normals* on Farnolith® administration (Table 3). Equally, parathyroid hormone, 1,25-dihydroxycholecalciferol and calcitonin did not alter significantly. In one test subject, however, we found a continuous, though slight increase in 1,25-dihydroxycholecalciferol. Phosphate and magnesium in the serum remained unaffected (Table 3). Calcium excretion decreased after one week and remained unchanged there after. The difference was not statistically significant, though (Table 3).

Citrate values increased slightly but not significantly. Phosphate-, magnesium- and oxalic acid excretion remained unaffected under Farnolith® therapy.

Calcium levels in the serum of patients suffering from *absorptive hypercalciuria type I* remained the same (Table 4). Parathyroid hormone values, which had been decreased before therapy, increased during Farnolith® treatment up to the limits of normal (Fig. 1). 1,25-dihydroxycholecalciferol and calcitonin did not change (Table 4). Calcium excretion decreased significantly after one month and remained in the upper range of normal during he study period (Fig. 3). Citrate, phosphate and magnesium values in the urine did not alter significantly (Table 4). In patients suffering from *renal hypercalciuria* parathyroid hormone and 1,25-dihydroxycholecalciferol values increased. Calcium excretion did not decrease. The other parameters remained unaffected.

Discussion

Our investigations have shown good results for patients suffering from absorptive hypercalciuria: calcium excretion returned to normal and oxaluria was reduced as well. The latter seems to be an important advantage of Farnolith® in comparison to sodium cellulose phosphate, which often causes hyperoxaluria. A considerable increase in citrate excretion, as described by Hesse [3] and Schneider [9], was not found. The share of magnesium in Farnolith® obviously prevented magnesium depletion. Our results demonstrate unchanged calcium homoestasis parameters in normals (calcium, parathyroid hormone, vitamin D metabolites). With patients suffering frm absorptive hypercalciuria, the parathyroid hormone values, which had been decreased before therapy, went back to normal, indicating a balanced calcium metabolism. As opposed to this, the patients suffering from renal hypercalciuria, showed an increase in parathyroid hormone and 1,25-dihydroxycholecalciferol indicating calcium deficiency. Investigations conducted by Langmann et al. [6] have shown that experimentally in-

duced calcium deficiency, caused by insufficient alimentary supply, produces a significant increase in 1,25-dihydroxycholecalciferol after 10 days.

Our investigation has shown that calcium homoeostasis parameters return to normalcy on administration of the dietary fibre Farnolith® in patients suffering from absorptive hypercalciuria type I; evidence of calcium depletion was not found with these patients and not with the normals either. Things are different, however, with primary renal hypercalciuria; here Farnolith® causes calcium depletion in the organism, as could be seen by the development of parathyroid hormone and 1,25-dihydroxycholecalciferol values.

Thus the ideal indication for Farnolith® is absorptive hypercalciuria, a disease which can not be changed for the better by low-calcium diet. In particular, Farnolith® does not produce secondary hyperoxaluria. Renal hypercalciuria (with secondary hyperparathyroidism) should not be treated with Farnolith. That is why calcium metabolism should be checked before and while administering Farnolith®.

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