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CRYSTALLINE DIHYDROTACHYSTEROL (DYGRATYL®) IN THE TREATMENT OF HYPOPARATHYROIDISM

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Abstract. Crystalline dihydrotachysterol has been used in the treatment of 26 patients with postoperative hypoparathyroidism. The clinical experience has been favourable. Dihydrotachysterol has advantages compared to calciferol, being faster in onset and fall-off of its effect, and can be given in an exact dosage. Hypercalciuria seems to be common, and urinary excretion of calcium should be determined regularly, as well as serum calcium.

Hypoparathyroidism has usually been treated with calciferol (vitamin D_2) or AT-10. Calciferol has the therapeutic disadvantage of an effect which is slow in onset and particularly in fall-off due to the long biological half-life. AT-10 consists of a mixture of irradiated sterols, dihydrovitamin D_2II —the isomer of dihydrotachysterol—being the chief component (8), and is standardized in equivalents of dihydrotachysterol. This standardization may vary by a factor of five (4).

It has been demonstrated in animals that crystalline dihydrotachysterol is more effective in raising serum calcium than calciferol (1) and, more important, has a more rapid effect and a considerably shorter biological half-life. These observations have been followed by clinical studies, and crystalline dihydrotachysterol has been successfully used in the treatment of hypoparathyroidism (4, 5), vitamin D deficiency (7, 6, 3), and vitamin D resistant rickets (5). The following report is concerned with our experience of crystalline dihydrotachysterol in the treatment of postoperative hypoparathyroidism.

MATERIAL

The clinical material consists of 23 females and three males between 22 and 75 years of age (Tables I and II). Three of the patients had had total parathyroidectomy because of generalized parathyroid hyperplasia. Six had had total thyroidectomy and 15 had had bilateral subtotal thyroidectomy. Two patients had had total hemithyroidectomy and subtotal thyroidectomy on the contralateral side with the lower part resected. In all patients the diagnosis of postoperative hypoparathyroidism was established on the basis of low serum calcium, often in combination with increased serum inorganic phosphate (Fig. 1). In 19 patients urinary excretion of calcium was determined and in three of these a roentgenologic survey of the abdomen was performed with regard to renal calcifications (Table II).

Crystalline dihydrotachysterol (Dygratyl from Philips through AB Ferrosan) was administered in tablets containing 0.1 and 0.2 mg.

Serum and urine calcium was determined with Eppendorf's flame photometer. Serum phosphate was determined as inorganic phosphate soluble in acid (2).

RESULTS

In the beginning of the study small initial dosages (0.2–0.4 mg/day) were given, which were gradually increased. In the later part a high initial dosage (1.0–2.0 mg/day) was given to achieve normal serum calcium more rapidly. When a normal serum calcium had been obtained the dosage was decreased until a satisfactory maintenance dosage was arrived at. The serum calcium was normalized in all patients, at a maintenance dose of crystalline dihydrotachysterol between 0.2 and 2.0 mg (Table II). With these dosages hypercalcemic episodes of short duration were observed in two patients (Figs. 2 and 3).

Hypercalciuria, which was defined as a urinary excretion exceeding 15 mEq/24 hours, was observed in seven of the 19 patients in whom determinations were performed. In three of the seven patients with hypercalciuria roentgenologic

Table I. *The clinical material with regard to type of surgery and clinical diagnosis*

Operation	Diagnosis	No. of pats.
Bilateral subtotal thyroidectomy	Non-toxic goitre	3
	Toxic goitre	12
Total thyroidectomy one side + subtotal contralateral	Non-toxic nodular goitre	2
Total thyroidectomy	Chronic thyroiditis	3
	Non-toxic nodular goitre	3
Total parathyroidectomy	General parathyr. hyperplasia	3
		26

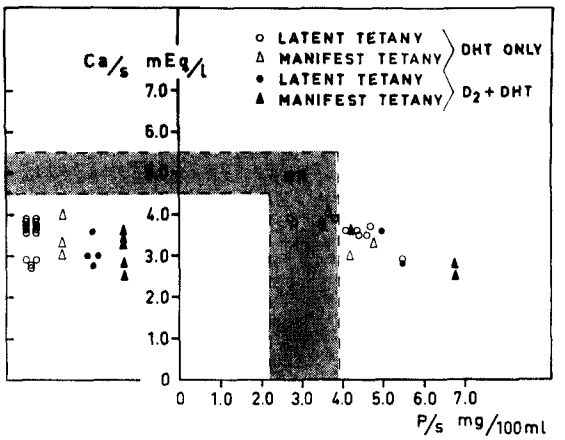

Fig. 1. Serum calcium ($n = 26$) and serum calcium correlated to serum phosphate ($n = 19$) before treatment of postoperative hypoparathyroidism was started either with calciferol (closed symbols) or crystalline dihydrotachysterol (open symbols). Circles indicate patients with latent tetany and triangles patients with frank tetany. Normal range for serum calcium 4.5–5.5 mEq/l, for inorganic phosphate 2.2–3.9 mg/100 ml.

surveys of the abdomen were made and did not reveal any renal calcifications.

Nine patients had previously been treated with calciferol. All nine declared that the treatment with crystalline dihydrotachysterol was easier to

Table II. *Duration of treatment, maximum and maintenance dosage, urinary calcium excretion and serum calcium at time of determination of urinary calcium*

Duration of treatment (months)	Pat.	Sex	Age (y.)	Maximum dosage (mg)	Maintenance dosage (mg)	Ca/u (mEq/24 h)	Ca/s (mEq/l)
3	A. K.	♀	59	1.2	0.2	—	—
4	L. F.	♀	34	1.6	1.2	—	—
5	G. O.	♀	37	0.8	0.8	11.9	4.3
5	A. A.	♀	55	1.0	0.8	15.3; 12.2	5.4; 5.0
6	A. M.	♀	28	2.0	2.0	17.6[a]	4.7
8	K. D.	♀	40	1.6	1.6	18.2; 19.1; 17.5[a]	4.6; 4.6; 4.6
8	E. A.	♀	56	0.8	0.8	2.3	5.2
9	S. R.	♂	44	0.4	0.4	5.0	4.9
10	T. S.	♂	22	1.3	0.8	14.5	4.9
11	S. S.	♀	75	0.8	0.8	—	—
12	S. Z.	♀	51	0.4	0.4	6.3	4.5
19	E. S.	♀	43	1.4	1.0	17.8; 19.0	5.3; 4.9
20	E. A.	♀	41	0.5	0.5	11.6	4.5
20	K. M.	♀	30	0.8	0.8	10.1	4.8
21	A. L.	♀	65	0.8	0.8	18.0	4.7
27	A. G.	♀	62	0.8	0.8	18.7	4.6
27	S. A.	♀	50	1.2	1.2	18.6	5.4
29	E. N.	♀	47	1.0	1.0	14.0	4.8
29	R. O.	♀	50	1.0	1.0	21.6; 19.3[a]	4.1; 5.0
29	H. P.	♀	30	0.6	0.6	11.0	4.5
29	W. S.	♂	35	0.5	0.5	6.3	4.8
29	E. N.	♀	74	0.4	0.4	—	—
30	S. B.	♀	39	0.6	0.5	—	—
32	S. D.	♀	62	0.6	0.5	—	—
34	I. C.	♀	33	0.4	0.4	—	—
34	A. H.	♀	52	0.5	0.3	11.0	5.1

[a] Patients who have had a roentgenologic survey of the abdomen; they showed no signs of renal calcification.

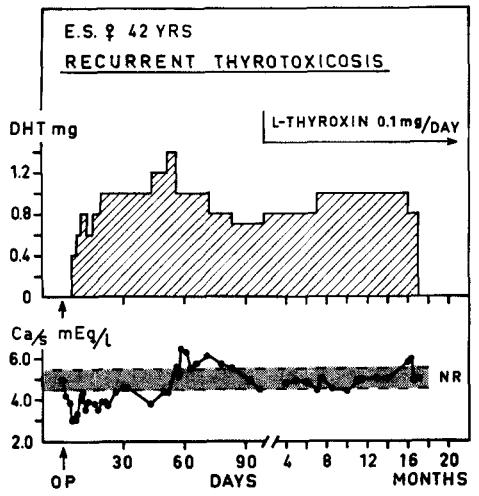

Fig. 2. The course of treatment with crystalline dihydrotachysterol in a patient with postoperative hypoparathyroidism after second operation for thyrotoxicosis. Note the rapid onset of the calcium-mobilizing effect and the rapid fall in serum calcium with reduced dosage. Normal range for serum calcium 4.5–5.5 mEq/l.

support and gave them a greater sense of well-being. However, only four had previously been in a reasonable steady state on calciferol. The calciferol dosages used in these four patients were 0.5, 1.2, 1.4 and 1.5 mg/day. A steady state was obtained with a dosage of dihydrotachysterol of 0.4, 0.8, 0.5 and 0.6 mg/day, respectively.

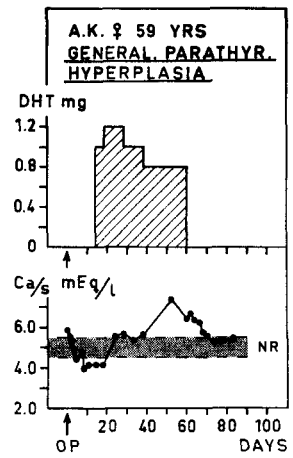

Fig. 3. The initial course of treatment with crystalline dihydrotachysterol in a patient from whom four enlarged parathyroids had been removed. Note the rapid fall in serum calcium when medication was stopped. Normal range for serum calcium 4.5–5.5 mEq/l.

DISCUSSION

Our studies confirm that crystalline dihydrotachysterol can successfully be used in the treatment of hypocalcemia due to postoperative hypoparathyroidism. The clinical experience has been favourable. In previous studies (4, 5) dihydrotachysterol has had a calcium-mobilizing effect 2–3 times that of calciferol. Our data are too few to permit a direct dosage comparison but seem to be in accord with previous findings.

Dihydrotachysterol has several advantages compared to calciferol. It is crystalline and can consequently be given in an exact dosage. The variations in dosage that necessarily occur in biologically tested therapeutic agents can be avoided. This is particularly important when dealing with potent substances. Dihydrotachysterol has an effect that is considerably faster in onset than calciferol and the biological half-life is shorter. This is illustrated by the rapid decrease in serum calcium in the two cases presented (Figs. 2 and 3).

Dihydrotachysterol is administered in tablets rather than a liquid solution. This is apt to reduce the number of mistakes regarding dosage. The patients generally found the tablets more convenient.

Crystalline dihydrotachysterol has been found to be more toxic in animal experiments than calciferol (1). This toxic effect was established on the basis of increase in serum creatinine and did not seem to correlate directly with the serum calcium level. A number of the patients reported here had hypercalciuria (>15 mEq/24 h) in spite of a normal serum calcium and without biochemical signs of renal damage. Consequently urinary excretion of calcium should be determined regularly and hypercalciuria should suggest a decrease in dosage of dihydrotachysterol.

In this study only patients with hypoparathyroidism were included. It seems, however, that dihydrotachysterol can replace calciferol in vitamin D deficiency (6, 3) and vitamin D resistant rickets (5). Harrison et al. (5) even observed that dihydrotachysterol is superior to calciferol in patients with steatorrhea. This observation may indicate that the gastrointestinal resorption of dihydrotachysterol is less affected than that of calciferol in patients with steatorrhoea.

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