been given in 14 years (13½ million of them during the first 3½ years).²⁸ Thus if iron compounds had any oncogenic properties they would be expected to be apparent by now.

Nevertheless, the regular development of sarcomas in some experimental animals raises the possibility of risk to other species. As with all bioassays for carcinogenicity, until the oncogenic mechanism has been defined and unless it is found inapplicable to man, the carcinogenic potential of iron compounds cannot be entirely discounted and must be considered a hypothetical hazard of treatment. The lack of epidemiological evidence, however, suggests that it is remote.

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Serum concentrations of 25-hydroxy vitamin D in Europeans and Asians after oral vitamin D₃

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Summary and conclusions

Serum concentrations of 25-hydroxy vitamin D (25-OHD₃) were measured in seven Asians of Indian extraction and eight Europeans before and at intervals after taking 1 mg vitamin D₃ by mouth. In all subjects the concentrations rose in the 24 hours after ingestion. There was little change over the next nine days in the concentrations in the Europeans but those in the Asians continued to rise until about day 10. Subsequent rates of fall in 25-OHD₃ were similar in the two groups.

Our observations suggest that the low serum concentrations of 25-OHD₃ found in Asians are not caused by either impaired intestinal absorption of vitamin D or rapid clearance of 25-OHD₃ from the plasma.

Introduction

Serum concentrations of 25-hydroxy vitamin D₃ (25-OHD₃) are lower in Asian immigrants in Britain than in the indigenous

white population, and although most Asians are asymptomatic, the abnormal alkaline phosphatase and parathyroid hormone concentrations suggest that many are deficient in vitamin D.¹⁻⁴ Ignorance about diet has been considered to be contributory,^{2, 5} though abnormally low concentrations have been found in Asian hospital staff, many of whom eat the same food as their English colleagues.⁴ Inadequate exposure to sunshine and impaired synthesis from 7-dehydrocholesterol in the skin on exposure to sunshine have also been suggested, though somewhat inconclusively.⁵⁻⁷ If skin synthesis is not the major factor and the intake of vitamin D₃ is essentially similar in whites and Asians^{2, 4, 5, 8} then genetic differences in vitamin-D absorption or metabolism may be responsible. We therefore measured the serum concentrations of 25-OHD₃ after vitamin D₃ by mouth in Asian and European subjects to determine possible differences in handling.

Subjects and methods

All subjects were professional staff at this hospital. The Europeans (five men aged 19-33 years, and three women) were randomly selected from volunteers whose serum concentrations of 25-OHD₃ were unknown. With one exception the Asian staff (five men, two women) were invited to participate because their serum concentrations were low.⁴ Blood samples were taken before and at intervals after ingestion of 1 mg vitamin D₃ in 300 ml milk one to two hours after lunch in July 1976. Fewer samples were taken from the women than the men. The subjects were asked only to avoid sunbathing and did not take holidays within six weeks after taking the vitamin D.

The initial blood samples were assessed for calcium, albumin, and alkaline phosphatase with the autoanalyser and for parathyroid hormone by the method of Addison *et al*.⁹ No abnormalities were found. 25-OHD₃ was measured by Ellis and Dixon's method.¹⁰

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Serum concentrations of 25-hydroxy vitamin D (25-OHD₃) measured before and at intervals after oral ingestion of vitamin D₃

Subject No	Sex	Race	Serum concentrations of 25-OHD ₃ (µg/l)*							
			Day 0	Day 1	Day 5	Day 9	Day 20	Day 46	Day 97	Day 191
1	M	European	33.4	38.9	38.6	34.6	33.1	24.6	19.1	13.0
2	M	"	26.5	28.7	30.6	28.8	28.3	27.7	21.4	11.1
3	M	"	24.3	28.0	28.6	29.7	24.6	19.4	13.1	9.0
4	M	"	50.9	57.4	59.0	54.8	54.3	38.7	24.0	13.0
5	M	"	37.1	42.0	42.6	42.9	34.8	34.0	30.6	21.5
6	M	Asian	6.8	14.4	21.7	21.4	19.6	17.3	9.9	4.9
7	M	"	5.0	17.9	25.8	25.6	22.8	18.3	10.6	4.3
8	M	"	3.5	12.0	18.8	18.7	16.6	12.0	5.7	3.7
9	M	"	3.6	11.6	17.3	19.4	20.0	13.1	5.4	3.5
10	M	"	10.2	17.1	22.8	21.7	21.4	22.8	14.6	7.1
11	F	European	19.4	28.6	29.4				17.1	9.7
12	F	"	24.7	30.8	28.6				14.3	11.8
13	F	"	37.4	48.3	49.1				30.0	14.9
14	F	Asian	3.6	8.4	14.3				7.0	4.6
15	F	"	5.8	12.9	17.7				11.7	8.1

*Conversion: 1 µg/l ≈ 2.6 nmol/l.

Results

The table gives the serum 25-OHD₃ concentrations before and at intervals for six months after ingestion of vitamin D₃. Mean concentrations in the men are shown in the figure. The concentrations in all

Mean serum 25-OHD₃ concentrations in Asian (●) and European (○) men after oral ingestion of vitamin D₃ 1 mg at day 0. Shaded areas are ranges. Conversion: 1 µg/l ≈ 2.6 nmol/l.

subjects rose rapidly in the first 24 hours. There was little change in the concentrations in the Europeans over the next nine days, but those in the Asians continued to rise until about day 10. The subsequent rate of fall was similar in both groups.

Discussion

The initial mean serum concentrations of 25-OHD₃ may have been higher in the Europeans because many of them had been sunbathing, and one (subject 4) had only recently been on holiday. Although no Asian had been sunbathing, subject 9 had played cricket weekly, and several others enjoyed outdoor pursuits. The immediate increase in serum 25-OHD₃ concentrations after the oral dose¹¹ contrasts with the 10-day lag reported by others.¹² Over the first five days the mean increase was greater in the Asians (14.3 µg/l) than the Europeans (6.6 µg/l), possibly due to suppression of D-25-hydroxylase activity by the higher initial serum concentrations.¹³

The rate of clearance of 25-OHD₃ from the serum has been thought to be exponential with time, the half-life varying between 13.3 and 20.7 days in normal people,¹⁴⁻¹⁶ 46.5 and 41.5 days in anephric patients,¹⁴ and 11 days in patients with osteomalacia.¹⁵ Others, however, have observed that the decline in serum concentrations is more linear than exponential.^{12 17} Thus

it may be more appropriate to describe the rate of fall in concentration over a particular period. In previous studies the daily decrease in concentration over days 10-46 after ingestion of 25 mg vitamin D₃ was 1.2 µg/l, and after 1 mg daily for 25 days the daily decrease over the next 35 days was 1.1 µg/l¹²; with higher initial concentrations (450-500 µg/l) it was approximately 2.2 µg/l.¹⁷ In our study the rates of fall over days 20-96 were much lower—namely, 0.14 µg/l in the Asians and 0.18 µg/l in the Europeans. This was possibly due to the lower initial concentrations. The greatest rate of fall (0.4 µg/l) occurred in subject 4, who had the highest initial concentration. It seems unlikely that the rates were greatly affected by synthesis in the skin, as sunbathing was avoided and our rates were comparable to those of 0.1 µg/l/day reported in nuclear submariners excluded from sunlight for two months.¹

Since crude dietetic assessment did not disclose any noticeable differences in vitamin D intake our data suggest that the low serum concentrations in Asians are not due to diet, impaired absorption of vitamin D₃, or rapid utilisation. Limited evidence suggests that skin synthesis is not impaired,⁷ and though many Asians avoid sunlight,¹⁸ some workers report equal exposure to sunshine in both Asians and European control groups.^{4 6 19} Nevertheless, it must be concluded that compared with Europeans, Asians either have a reduced intake of vitamin D₃ or are exposed less to sunshine or synthesise vitamin D₃ from such exposure less effectively. Clearly, much work still remains to resolve the problem.

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