time had been stable in the therapeutic range (two to three times control) taking 6 mg warfarin daily. He discontinued his carbamazepine, and when seen four weeks later his prothrombin time was five times control. He subsequently required 4 mg warfarin daily to maintain his prothrombin time at two to three times control. Some months later he started taking carbamazepine 300 mg daily again. The prothrombin time was measured weekly and his warfarin dose adjusted as necessary. His serum γ-glutamyl-transferase (γ-GT) concentration was also measured weekly. His warfarin requirements increased from 3·5 mg daily to 5·5 mg daily over a period of five weeks and his serum γ-GT rose from 11 U/l to 27 U/l during the same period. The effects of carbamazepine on warfarin dose and γ-GT are shown in the figure.

Comment

Stopping carbamazepine considerably increased the effect of warfarin on the prothrombin time in this patient and restarting carbamazepine reduced the effect of warfarin, taking five weeks to reach a steady state. Hansen *et al* showed that giving carbamazepine to patients already taking warfarin lowered serum warfarin concentrations and warfarin half life.[3] Warfarin is hydroxylated by hepatic microsomal enzymes,[3] and Whitfield *et al*[4] showed that changes in γ-GT may reflect changes in the activity of liver cell microsomal enzymes. The results in our patient suggest that this interaction may be clinically important and is probably due to increased warfarin metabolism produced by carbamazepine.

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Comparison of serum 25-OH vitamin D concentrations in rheumatoid arthritis and osteoarthrosis

While occasionally there may be radiological evidence of osteomalacia in rheumatoid arthritis[1] and histological osteomalacia may be found in some patients with rheumatoid arthritis and bone pain,[2] the exact state of vitamin D metabolism in this disease remains uncertain. In a recent series of 23 patients with rheumatoid arthritis there was no biochemical evidence of osteomalacia and serum 25-hydroxy vitamin D (25-OHD) concentrations were within the normal range.[3] Since serum 25-OHD concentrations can be affected by medication and lack of sunlight exposure owing to immobility, we have compared the concentrations in 30 patients with rheumatoid arthritis and 30 patients with osteoarthrosis, all sufficiently severe to be admitted to hospital, to show any alterations caused by rheumatoid arthritis.

Patients, methods, and results

We studied 60 consecutive patients admitted to the Royal Bath Hospital, Harrogate: 30 had classical or definite rheumatoid arthritis (ARA criteria) and 30 had osteoarthrosis (moderate or severe osteoarthrotic changes on *x*-ray examination, normal erythrocyte sedimentation rate (ESR), and negative serology for rheumatoid factor). Both groups were bled in the fasting state concurrently between November and December 1978 on the first day of admission to hospital. Blood was measured for full blood count, ESR, calcium, liver function tests, rheumatoid factor, and plasma 25-OHD.[4] A dietary survey was made and exposure to sunlight quantified by a questionnaire and simple scoring system.[5] Patients in the two groups were well matched for age, sex, duration of arthritis, exposure to sunlight, and dietary vitamin D intake (table). Details of drug treatment, including non-steroidal anti-inflammatory agents (NSAIA), for both groups are also shown in the table.

Comparisons in patients with osteoarthrosis and patients with rheumatoid arthritis (means ± SD)

	Osteoarthrosis (n = 30)	Rheumatoid arthritis (n = 30)
Mean age (years)	63·3 ± 15·0	60·8 ± 9·5
Sex (M:F)	8:22	10:20
Mean duration of arthritis (years)	12·7 ± 8·9	13·7 ± 9·8
Mean sunlight exposure score[5]	25·1 ± 10·5	23·2 ± 11·4
Mean dietary vitamin D intake (IU/day)	240 ± 185	234 ± 154
Plasma 25-OHD concentration (mmol/l)*	40·13 ± 43·27	59·33 ± 51·58
No receiving one analgesic	14	18
No receiving two analgesics	4	—
No receiving one NSAIA	17	19
No receiving more than one NSAIA	3	7
No receiving Myocrisin	—	10
No receiving penicillamine	—	2

*Normal range 12·5 mmol/l-181·25 mmol/l.
NSAIA = Non-steroidal anti-inflammatory agent.
Conversion: SI to traditional units—Plasma 25-OHD: 1 mmol/l ≈ 0·4 mg/ml.

The difference between the mean plasma 25-OHD concentration in rheumatoid arthritis (59·33 mmol/l (23·73 mg/ml)) and in osteoarthrosis (40·13 mmol/l (16·05 mg/ml)) was not significant. A reduction in 25-OHD concentrations was seen with age in both groups. There was no significant difference between the groups in any biochemical value measured, though the alkaline phosphatase was slightly higher in the rheumatoid group (11·87 units against 9·15 units)—a difference probably attributable to the activity of the rheumatoid disease. No significant correlations were seen between 25-OHD concentration and duration of arthritis or articular index in the rheumatoid group, though there was a trend to an inverse correlation in this group between 25-OHD and ESR ($0·1 > p > 0·05$). Analysis of questionnaires showed that sunlight exposure was more important than dietary vitamin D in determining 25-OHD state in both groups.

Comment

Since the 25-OHD concentrations were measured in winter before the patients had been exposed to a hospital diet or fluorescent light their plasma 25-OHD was probably at its lowest annual value and osteomalacia at its most obvious. The two groups were well matched for all factors that might have altered vitamin D metabolism, apart from the type of arthritis. Nevertheless, there was no significant difference in their 25-OHD concentrations and the mean value in the rheumatoid arthritis patients was similar to that recently reported (68·7 mmol/l) by Kennedy *et al*.[3]

We have found no evidence of biochemical osteomalacia in rheumatoid disease, and although osteomalacia may occasionally occur it probably does so coincidentally. 25-OHD concentrations fell with age in both groups, as they would in a normal population. The possible association between 25-OHD and ESR in rheumatoid disease deserves further study, though we have found no evidence that systemic 25-OHD concentrations relate to the degree of juxta-articular osteopenia that differentiates rheumatoid arthritis from osteoarthrosis.

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