Previous investigations have shown that the antiandrogen cyproterone acetate produces identical results in the same experimental procedure, while the non-hormonal sebosuppressive agent benzoyl peroxide influences the parameters mentioned partly in a different manner (2, 8). This allows the assumption that cimetidine exerts its sebosuppressive effect through an antiandrogenic mechanism.

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Vitamin A Transport Complex during Treatment with an Oral Aromatic Retinoid (RO 10-9359)

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Abstract. No significant changes were noted in the serum levels or molar ratios of vitamin A, retinol-binding protein (RBP) and prealbumin even during long-term (up to 15 months) treatment with RO 10-9359 in 19 patients with normal renal function. Nor did any significant alteration occur in the highly significant correlations between vitamin A and RBP, and between RBP and prealbumin. In 3 patients with slightly elevated serum creatinine, some tendency towards an elevation of vitamin A and RBP levels was seen.

Key words: Aromatic retinoid; Vitamin A transport complex; Retinol-binding protein; Prealbumin

Vitamin A is known to control the growth and differentiation of epithelial tissues (4). New synthetic retinoids (analogs of vitamin A), especially an aromatic retinoid (RO 10-9359), have proved to be effective in the treatment of psoriasis and keratinization disorders (3, 4).

Studies with radioactive RO 10-9359 have shown that, after oral administration, 75% of the dose can be detected in faeces (most of it excreted by bile) and 12% in the urine within 8 days (2). In view of the slow excretion, some accumulation obviously occurs. This is supported by the clinical experience of prolonged action (3).

Many side effects of the aromatic retinoid, such as dryness of the mucous membranes, desquamation of the skin and loss of hair, are also seen after prolonged overdosing with vitamin A. They are obviously general side effects of retinoids which may be produced without interference with vitamin A metabolism. In order to test this theory the serum levels of vitamin A, retinol-binding protein (RBP) and prealbumin, which are known to form the transport complex of vitamin A (9, 10, 11), were monitored during treatment with the aromatic retinoid.

MATERIALS AND METHODS

The serum levels of vitamin A, retinol-binding protein (RBP) and prealbumin were repeatedly determined in 22 patients before and during treatment with an oral aromatic retinoid (RO 10-9359). There were 18 men and 4 women; weight: 73.1±10.8 kg (mean ± S.D.); age: 44.4±17.8 years. The diseases of the patients included psoriasis in 14, PRP in 3, linear porokeratosis in 1, Mb. Darier in 1, erythrokeratodermia variabilis in 1, and ichthyosis congenita in 2 cases. The initial retinoid dose was 0.80±0.11 (mean ± S.D.) mg/kg body weight. The dose was later reduced gradually according to the patient's response. During the treatment period from 2 to 5 months the dose was 0.60±0.26 (mean ± S.D.) mg/kg and 0.39±0.13 mg/kg after 9 months of treatment. The monitoring periods ranged from 2 weeks to 15 months, depending on the duration of the treatment. Serum transaminases, alkaline phosphatase and creatinine were checked simultaneously.

Serum vitamin A level was measured by the method described by Paterson & Wiggins (8). RBP and prealbumin were determined by a single radial immunodiffusion method using LC-Partigen immunodiffusion plates for RBP, and M-Partigen immunodiffusion plates for prealbumin quantitation (manufactured by Behringwerke AG, Marburg, W. Germany). Normal ranges given by the manufacturer are 30–60 mg/l for RBP and 100–400 mg/l for prealbumin.

The following molecular weights were used for the calculation of molar ratios: RBP 21 000, prealbumin 49 400 (10) and vitamin A 286.44 (1). Statistical significance was tested by Student's *t*-test or analysis of variance.

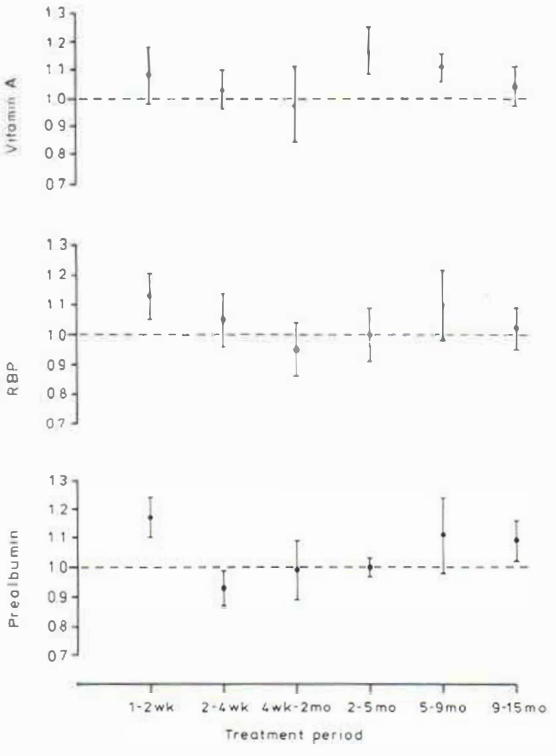

Fig. 1. The relative serum levels (during/before treatment) of vitamin A, RBP and prealbumin during treatment with RO 10-9359. Each point represents the mean ± S.E.M. of 6–11 samples collected during the respective treatment period.

RESULTS

Neither the serum levels of vitamin A, RBP and prealbumin nor the molar ratios of RBP: vitamin A and RBP: prealbumin showed any significant change during treatment with RO 10-9359 in 19 patients with normal renal function (Table 1). Prior to treatment there was a highly significant correlation between serum levels of vitamin A and RBP ($r=0.70$, d.f. 17, $p<0.001$) and between RBP and prealbumin ($r=0.78$, d.f. 17, $p<0.001$). No significant change occurred in these correlations during treatment. When measured at various times during treatment, the serum level ratios (during/before treatment) of vitamin A, RBP and prealbumin (Fig. 1) and also the relative levels of the molar ratios of RBP: vitamin A and RBP: prealbumin (Fig. 2) showed only a non-significant fluctuation (analysis of variance, one-way classification) with no definite trend towards deviation from initial levels.

There were 3 patients with signs of slightly impaired renal function. Patient U. L. (severe psoriasis) had a creatinine level of 130 μmol/l before treatment; during treatment, levels up to 155 μmol/l were detected. In patient A. H. whose pretreatment

Table 1. *The serum levels (mean ±S.E.M.) of vitamin A, RBP and prealbumin (PA) and the molar ratios of RBP: vitamin A and RBP: PA before and during treatment with RO 10-9359 in 19 patients with normal renal function*

	Number of samples	Vitamin A (μmol/l)	RBP (mg/l)	PA (mg/l)	RBP: vitamin A	RBP: PA
Before treatment	19	1.54±0.09	49.7±2.5	259±18	1.62±0.07	0.45±0.02
During treatment	43	1.56±0.05*	48.8±1.2*	265±9*	1.54±0.05*	0.44±0.01*

* Difference not significant (Student's *t*-test).

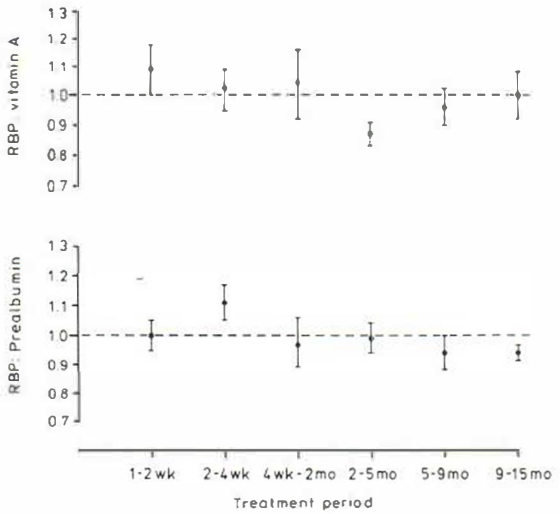

Fig. 2. The relative molar ratios (during/before treatment) of RBP: vitamin A and RBP: prealbumin during treatment with RO 10-9359. Each point represents the mean ± S.E.M. of 6–11 samples collected during the respective treatment period.

level was 93 μmol/l, the creatinine fluctuated, with a peak of 135 μmol/l. Administration of RO 10-9359 to patient L. V. had to be discontinued because of oedema. Shortly after the cessation of treatment his creatinine level was 120 μmol/l; the pretreatment level had been 74 μmol/l.

In these 3 patients the pretreatment levels (mean ± S.E.M.) of vitamin A, RBP and prealbumin were 1.67±0.20 μmol/l, 55.7±6.7 mg/l and 349±84 mg/l, respectively. In 13 samples taken during treatment the serum level ratios (during/before treatment) were as follows: vitamin A 1.36±0.15 (mean ± S.E.M.), RBP 1.30±0.04 and prealbumin 0.96±0.06. Thus the levels of vitamin A and RBP showed some tendency to elevation.

DISCUSSION

The initial levels of RBP and prealbumin in our patients closely resemble those previously reported (10, 11). The initial vitamin A level was somewhat lower than those of Smith & Goodman, 1.75±0.05 μmol/l (10) and Mier et al., 1.89 μmol/l (6). This may have resulted from the different assay method and apparently also from differences in dietary habits. Consequently, our molar RBP: vitamin A ratio was somewhat higher than that of Smith & Goodman (10). It has been found in previous studies that vitamin A levels in the diseases included in our study do not differ significantly from control values (5, 6).

RO 10-9359 is an aromatic ethyl ester of retinoic acid. After oral administration it is hydrolysed in the gut, liver and blood to a corresponding acid (RO 10-1670) which is excreted into the bile; various metabolites with shortened side chains have been found in the urine (2). The results of the present study show that there is no significant interference with the vitamin A level or transport in blood during even long-term treatment with RO 10-9359 in patients with normal renal function. This is important, since toxic accumulation of vitamin A might otherwise occur.

Patients with impaired renal function have been found to have elevated levels of vitamin A and RBP (10, 11). The RBP level in these patients is obviously elevated because of accumulation of apo-RBP, which does not contain vitamin A (10, 11). The higher levels of vitamin A and RBP seen in 3 patients during treatment may thus be a consequence of weakened glomerular filtration reflected as elevated levels of serum creatinine. Whether or not the elevation of creatinine in patients A. H and L. V. was caused by the treatment cannot be established with certainty. Later during treatment the creatinine level reverted to normal in patient A. H., which speaks against this supposition. On the other hand, in a large multicentre study, elevation of creatinine has been noted in some patients, though not with any statistical trend (7).

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The Effect of Benzoyl Peroxide on Acne

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Abstract. A double-blind study of two commonly used (5%) benzoyl peroxide-containing preparations showed that they were equally effective in the treatment of acne. With these treatments there was a reduction in *P. acnes*, Micrococcaceae and surface-free fatty acids. These data support the continued use of benzoyl peroxide preparations in the treatment of acne.

Key words: Acne; Benzoyl peroxide; Free fatty acids; *P. acnes*

An effective treatment of acne based on anti-bacterial action can be demonstrated by a reduction in the number of acne lesions, a reduction in the cutaneous microflora and a reduction in the amount of free fatty acids in the surface lipid as a consequence of diminished bacterial lipase activity.

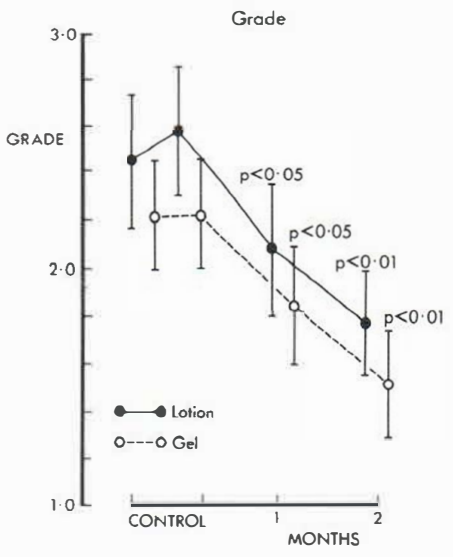

Fig. 1. The effect of therapy on acne grade.

Benzoyl peroxide has been shown to have anti-bacterial activity against *Propionibacterium acnes* (*P. acnes*) (3). The efficacy of a topically applied drug depends partly on its percutaneous absorption and vehicle. We have compared two commonly available preparations of benzoyl peroxide by monitoring their clinical effect on acne and the effect on the cutaneous bacterial flora and free fatty acids in surface lipids.

MATERIALS AND METHODS

The trial was carried out between January and April. The subjects chosen were 48 student volunteers with acne of a mild to moderate severity. They were aged 18–22 years; 28 were females and 20 were males. They had not been on any topical or oral therapy for acne vulgaris for 6 weeks.

Table 1. *Percentage of incidence of side effects in patients*

	1 month	2 months
Erythema		
Lotion	29	40
Gel	24	24
Scaling		
Lotion	33	21
Gel	25	8