cell systems can be inhibited in vitro by increased intracellular cyclic AMP levels (6). The inhibition of catechol-O-methyltransferase by pyrogallol results in an accumulation of catecholamines in the treated areas. Such an accumulation will increase the intracellular cyclic AMP levels via stimulation of adenylcyclase (7).

It seems worth while to investigate the effectivity of this drug in a series of patients with mycosis fungoides. An extra therapeutic modality for stubborn cases would be of great practical value.

ACKNOWLEDGEMENT

The author wishes to thank Professor J. W. H. Mali for his advice to keep in mind therapies from many decades ago.

REFERENCES

1. Baker H, Wilkinson DS. Psoriasis. In: Rook A et al., eds. Textbook of dermatology. Oxford: Blackwell Scientific Publications, 1979; 1315–1368.
2. Edelson RL. Cutaneous T cell lymphoma: Mycosis fungoides, Sézary syndrome, and other variants. J Am Acad Dermatol 1980; 2: 89–106.
3. Thomsen K, Molin L, Volden G, Lange Wantzin G. 13-cisretinoic acid effective in mycosis fungoides. Acta Derm Venereol (Stockh) 1984; 64: 563–566.
4. Claudy AL, Rouchouse B, Boucheron S, Le Peptid JC. Treatment of cutaneous lymphom with etretinate. Br J Dermatol 1983; 109: 49–56.
5. Ackermann H. Die kalorigene Wirkung von Adrenalin ohne und nach Vorbehandlung mit Pyrogallol und Desipramin. Biomed Biochem Acta 1984; 3: 395–400.
6. Voorhees JJ, Duell EA, Kelsy WH. Dibutyl cyclic AMP inhibition of epidermal cell division. Arch Dermatol 1972; 105: 384–386.
7. Gomman JM, Bergers M, van Erp PEJ, van de Hurk JJMA, van de Kerkhof P, Mier PD, Roelfzema H. Studies on the plasma membrane of normal and psoriatic keratinocytes. 2. Cyclic AMP and its response to hormonal stimulation. Br J Dermatol 1979; 101: 413–419.

Vulval Lichen sclerosus et atrophicus Treated with Etretinate (Tigason®)

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Mørk NJ, Jensen P, Hoel PS. Vulval lichen sclerosus et atrophicus treated with etretinate (Tigason®). Acta Derm Venereol (Stockh) 1986; 66: 363–365.

In an open uncontrolled study eight patients with vulval lichen sclerosus et atrophicus were given etretinate (Tigason®) 1 mg/kg/day. The dose was then gradually reduced according to effect and side effects. Six patients showed improvement in symptoms and in clinical morphology based on the physician's evaluation and photograpic documentation. In four of five patients where biopsies were taken, there was a marked change in the histological picture towards normalization. Two patients did not respond to the treatment. All patients experienced the well-known side effects of etretinate in various degree. We conclude that treatment with etretinate should be tried in vulval lichen sclerosus et atrophicus if the result of other therapeutical efforts are unsatisfactory. (Received February 13, 1986.)

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Lichen sclerosus et atrophicus in women is commonly restricted to the perigenital region. Treatment for this condition is most unsatisfactory. Many patients suffer from itching and burning sensations giving difficulties in their sexual and marital relations.

Etretinate (Tigason®) is widely used for treatment of keratinizing disorders (1). Encouraged by the work of Romppanen & Tuimala (2) reporting effect with etretinate in vulval dystrophy we decided to do an open pilot study of etretinate treatment of vulval lichen sclerosus et atrophicus.

MATERIAL

Eleven patients were asked to enter the study. Eight patients accepted. The age of these eight patients varied from 21–63 years (mean 47.4 years). They all had a history of vulval symptoms including itching, burning sensations and dyspareunia for 3–20 years (mean 9.6 years). The diagnosis of lichen sclerosus et atrophicus had been made 1 to 13 years earlier (mean 4.3 years). All patients had intermittently been treated with various topical preparations, mostly corticosteroids and antiseptics. Three patients had undergone partial vulvectomia. All treatment had no or minimal effect.

Approximately 1 mg/kg/day etretinate was given as starting dose and then gradually reduced based on the clinical consideration of effect and adverse reactions. No other systemic or topical medication was given during he study except local application of emollients.

The patients were examined regularly during the treatment. They were asked for changes in symptoms and for side effects. The lesions were clinically evaluated and were photographed before start of treatment and at follow-up visits. All patients were biopsied before entering the trial and most patients also at one or two follow-up visits with emphasis on taking the biopsies from the same and most affected area. The patients have been followed for 39–46 weeks.

RESULTS

Six of our eight patients reported improvement of symptoms. This improvement was found to be parallel with a clinical morphological improvement based on the physician's evaluation and on the photographic documentation. Biopsies were taken from five of these six patients. Four showed histological signs of normalization, while one did not reveal any significant change.

Previous to the given treatment the four patients had histological findings typical of the late stage of lichen sclerosus et atrophicus, including various degree of hyperkeratosis and a prominent thickening of the papillary dermis by sclerosis and almost hyalinization with a few fibroblasts and telangiectases. Beneath the sclerotic dermis there was a slight inflammatory infiltrate composed of lymphomonocytic cells, partly perivascular, partly band-like. At the dermoepidermal junction edematous/vacuolar alteration of the basal cells was evident, occasionally with the formation of small clefts. After approximately 17 weeks treatment all these changes were reversed towards normal. One patient merely showed the picture of a chronic unspecific dermatitis 17 weeks after start of therapy, while the other three still had persistent, small edema zones in the uppermost dermis.

On disappearance of symptoms after 14 and 18 weeks respectively two of the six patients stopped treatment. One patient greatly improved but stopped treatment after 18 weeks because of side-effects. These three patients did not experience any flare-up. Three of the six patients had to continue treatment on a reduced dose to control symptoms.

Two of our eight patients aged 21 and 34 stopped the treatment after 12 and 10 weeks due to lack of improvement and side-effects. These two non-responders had a five- and ten-year history of perigenital pruritus respectively. Lichen sclerosus et atrophicus was diagnosed in 1983 in both cases. The six patients who reported improvement were aged 42–63 (mean 53.3 years) with a similar 3- to 20-year long history of symptoms (mean 10.3 years). Lichen sclerosus et atrophicus had been diagnosed 3–13 years earlier (mean 4.0 years).

All patients experienced the characteristic side-effects of etretinate in various degree.

DISCUSSION

The improvement seen in six of eight patients in this open uncontrolled study could be verified by clinical evaluation, photograpic documentation and histological examination. The fact that those patients who reported improvement were older than the non-responders and had had the disease for a longer time, could be explained by a possible greater tolerance of side-effects, less expectations and greater patience often found in older patient populations.

It is rather well documented that lichen sclerosus et atrophicus has a relationship to auto-immune disease (3) and that the retinoids have several effects on the immune system (4). There is also evidence for anti-inflammatory activity of etretinate and in this way it exerts distinct therapeutic effects on various skin diseases with dermal inflammatory involvement (5). Hein et al. (6) have shown that collagen production and the synthesis of non-collagenous proteins were reduced with increasing concentrations of etretinate and various retinoid analogues. These different effects of etretinate may contribute to the fact that some patients with lichen sclerosus et atrophicus show improvement on etretinate treatment.

In an open, uncontrolled pilot study including 8 patients with various subtypes of lichen sclerosus et atrophicus, Neuhofer & Fritsch (7) concluded that only moderate therapeutic effects can be achieved with etretinate. Allevato et al. (8) reported clinical improvement of etretinate in five patients with lichen sclerosus et atrophicus. In some of these patients a histological improvement was seen, but the lack of international experience was stressed. Romppanen & Tuimala (2) reported effect of etretinate treatment in thirteen women with vulvar dystrophy, i.e. keratotic changes of the vulva including lichen sclerosus et atrophicus, leukoplakia and pruritus.

The present study shows improvement in six of eight patients with vulval lichen sclerosus et atrophicus treated with etretinate. We conclude that this drug should be tried if the result of other therapeutical efforts are unsatisfactory.

REFERENCES

1. Peck GL, Yoder FW. Treatment of lamellar ichthyosis and other keratinising dermatoses with an oral synthetic retinoid. Lancet 1976; ii: 1172–1174.
2. Romppanen U, Tuimala R. Etretinate treatment of vulvar dystrophia. Acta Obstet Gynecol Scand 1983; Suppl 116: 39.
3. Harrington CI, Dunsmore IR. An investigation into the incidence of auto-immune disorders in patients with lichen sclerosus et atrophicus. Br J Dermatol 1981; 104: 563–566.
4. Shapiro PE, Edelson RL. Effects of retinoids on the immune system. In: Saurat JM, ed. Retinoids: New trends in research and therapy. Basel: Karger, 1985: 225–235.
5. Orfanos CE, Bauer R. Evidence for antiinflammatory activities of oral synthetic retinoids: Experimental findings and clinical experience. Br J Dermatol 1983; Suppl 25: 55–60.
6. Hein R, Mensing H, Müller PK, Braun-Falco O, Krieg T. Effect of vitamin A and its derivatives on collagen production and chemotactic response of fibroblasts. Br J Dermatol 1984; 111: 37–44.
7. Neuhofer J, Fritsch P. Treatment of localized scleroderma and lichen sclerosus with etretinate. Acta Derm Venereol (Stockh) 1984: 64: 171–174.
8. Allevato MAJ, Itala JH, Donatti LB, Di Paola GR, Rueda NMG, Cordero AA. Tratamiento del liquen escleroso y atrofico de vulva con el derivado aromatico del acido retinoico. RO10-9359. Actualizaciones Terapeuticas Dermatologica 1983; 3: 145–157.