

DARIER'S DISEASE: RESPONSE TO COMBINATION OF VITAMINS A AND E

Kader Naina Mohamed

SYNOPSIS

Identical twin sisters with Darier's disease were successfully treated with a combination of oral vitamins A and E after vitamin A alone in a higher dose did not yield a good response. Although synthetic retinoids are currently favoured drugs for disorders of keratinization, the usefulness of the synergistic action of these fat-soluble vitamins is recapitulated and the lack of side-effects while the therapeutic dose far exceeds the normal requirement is emphasized.

INTRODUCTION

In 1913, Osborne and Mendel, McCullum and Davis isolated vitamin A (1) which is not synthesized by the body. Vitamin A is essential for many biological functions such as growth, vision, reproduction and maintenance of epithelial cells. In 1936, Evan and colleagues isolated vitamin E from wheat-germ oil. The physiological action is presumed to prevent the destruction of non-enzymatic oxidation of poly unsaturated fatty acids. Vitamin A has been used for the treatment of acne vulgaris, Darier's disease, pityriasis rubra pilaris and ichthyosis. But the initial dose of 50,000 IU to 100,000 IU was ineffective and higher dose in the region of 300,000 IU to 500,000 IU had to be given when apprehension over systemic side-effects restricted its use. Its significance was reawakened when it was shown that experimental rats whilst fed on a diet deficient in Vitamin E were found to have a drop in the vitamin A level which was promptly reinstated after vitamin E was administered, proving synergism between these two vitamins (2). Although many of us would have used vitamin A in the treatment of various disorders, published reports from this region on the simultaneous use of these vitamins are lacking. This paper describes twin sisters who responded well to this combination.

Department of Dermatology
Sultanah Aminah General Hospital
80100 Johor Bahru
Malaysia

K N Mohamed, MBBS (Madras), Dip Derm
(Lond), Dip Ven (Lond)
Consultant Dermatologist

CASE REPORT

A 29-year old monozygous Malay twin woman (3) was seen at the skin clinic with small, firm papules over the face and neck of 15 years duration (Fig. 1). Histopathological examination of the skin confirmed the clinical diagnosis of Darier's disease in both the twins. These spinsters who attained menarche at the age of 13, were previously treated with short courses of injection of vitamin A 100,000 IU daily at irregular intervals for about 2 years without satisfactory response. They were planned for systemic therapy with vitamins A and E. Since they presented with persistent headache over the occipital region not responding to analgesics, thorough investigations including computed tomography (CT) scan of the skull were carried out but did not reveal any organic basis for the headache.

Routine investigations such as full blood picture, ESR, liver function tests, total lipids, blood urea and serum electrolytes were within normal limits. Fundus oculi of both showed myopic changes. They were

started with vitamin A 100,000 IU in the form of axerophthal (Roche) and vitamin E 1,600 IU in the form of d-alpha tocopherol derived from natural vegetable oil (Abbott) daily. Within two months of therapy there was marked improvement. The papular lesions over the sides of the neck became flat followed by those over the face (Fig. 2). Photosensitivity became much less and they were able to carry out their normal activities with ease and comfort. There was no undesirable side-effects such as anorexia, cheilitis, malaise and hair loss. Later the dose was reduced and maintained with daily vitamin A 50,000 IU and vitamin E 800 IU. After one year of treatment they remained well and there was no evidence of papilloedema. Their body weight increased from 31 Kg to 38 Kg. The lipid analysis was within normal limit. There was convincing evidence of clinical remission after eight months of low, maintenance dose of these vitamins and therefore treatment was stopped for fear of inducing hypervitaminosis A on prolonged therapy. For the past four months they are under observation without treatment and also without relapse of the lesions.



Figure 1. One of the twin sisters with papular lesions over the side of the neck and face before treatment.

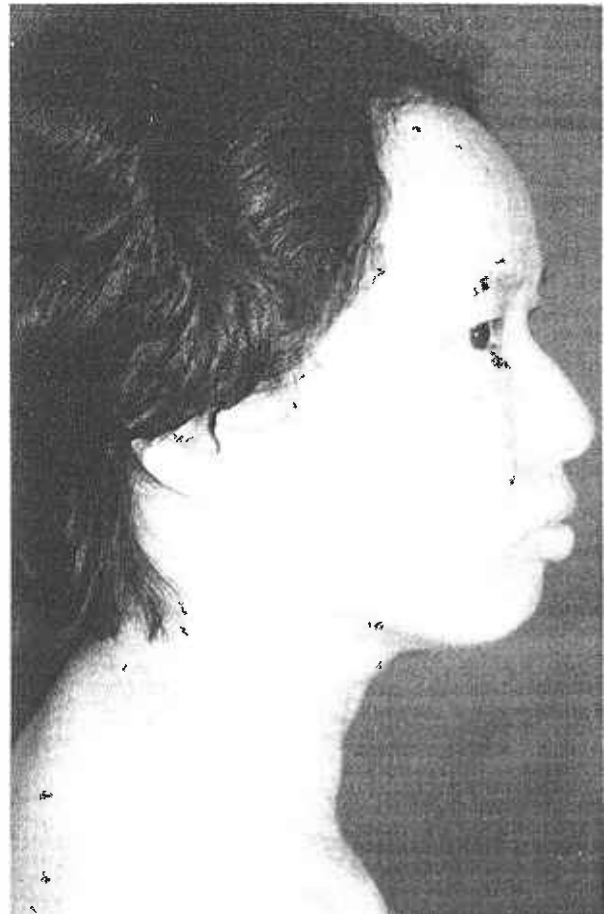


Figure 2. Disappearance of lesions leaving hypo-pigmented spots one year after combined therapy with vitamins A and E.

DISCUSSION

Vitamin A activity is carried out by three major compounds. They are:- a) Retinol — Vitamin A alcohol which is the dietary and storage form. b) Retinal — Vitamin A aldehyde formed from retinol by reversible dehydration and which is necessary for night-vision. c) Retinoic acid — Vitamin A acid which is formed by irreversible oxidation of retinol and which retains most functions of vitamin A except that it is not stored in the liver and has no role in reproduction and visual cycle. The synthetic analogues of retinoic acid have made major break-through in the treatment of various defects of keratinization (4). The role played by vitamin A in the formation of visual purple (rhodopsin) is well established but the mechanism regulating other functions is not known. Perhaps it may act as a carrier for the carbohydrate necessary for the cells.

Vitamin A was used for Darier's disease following an earlier hypothesis that it was due to the deficiency of the vitamin (5). Since there was therapeutic response (5) it was used with variable success along with topical tretinoin. After the discovery of Ames (2) that vitamin E enhanced utilization of vitamin A six times, combined administration of vitamins A and E was tried with favourable result (6). Later, the magnificent discovery of oral retinoids has become the popular choice for the treatment of this disorder (7).

The twin sisters reported here responded well to the initial dose of oral vitamin A 100,000 IU and vitamin E 1,600 IU within two months of uninterrupted therapy. These patients were well motivated and their compliance to therapy much to be appreciated. The rough texture of the skin became smooth, less hyperpigmented and subsequently replaced by hypopigmented spots (Fig. 2). They remained in remission even in hot and humid weather, at times of emotional turbulence and after many hospital admissions for investigations.

The photosensitivity was markedly reduced within four months of therapy. They did not develop cheilitis which is a frequent side-effect of retinoids. The headache, although persistent was not exacerbated after therapy. Several authors have warned against the toxic effects of vitamin A when it exceeded well above the physiological need of 5,000 IU. But Kligman and his colleagues found that the signs of hypervitaminosis A are exaggerated and xerosis and cheilitis

were mild even at a dose of 400,000 IU to 500,000 IU of vitamin A (8). In the limited trial, the author finds the combination of vitamins A and E most encouraging. Currently, they are closely followed-up during this period of remission. Should a relapse occur, they may be restarted with oral vitamins A and E or topical tretinoin (9) as the clinical condition warrants.

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