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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.
ORAL VITAMIN A ACID IN TREATMENT OF DERMATOSES WITH PATHOLOGIC KERATINIZATION

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Detailed acute and chronic toxicity studies of Vitamin A acid suggest that repeated daily doses of 20 to 30 mg may be tolerated. The toxic dosages obtained in animals were also confirmed in our investigations with humans, where daily oral doses of 50 to 100 and 200 mg Vitamin A acid caused side effects. Common side effects include headache, anorexia, dryness of lips and skin, and fatigue. Other less common findings include nausea, polydipsia, changes in pruritus, dizziness, hyperventilation and petechia. Side effects encountered with oral Vitamin A acid at doses of 100 mg corresponded to those observed at high doses of Vitamin A palmitate. One mg of Vitamin A acid is equivalent to 2,500 IU Vitamin A palmitate or 3,300 IU of Vitamin A alcohol; 100 mg Vitamin A acid corresponds to 3,000,000 IU of Vitamin A.

Results in Treatment of Dermatoses

Acne Vulgaris
The treatment of acne vulgaris seemed to be a suitable model for studies of the effects of oral use of Vitamin A, since the effects of local application, such as the loosening of comedones and decrease of papulopustular efflorescences, yields quantitative data. Five to 10 mg Vitamin A acid represents the highest effective concentration tolerated by patients during long-term therapy without side effects.

We chose these patients for oral Vitamin A acid treatment because they did not show satisfactory improvement after prolonged topical treatment. They continued topical treatment and were given Vitamin A acid per os. If there was a marked improvement with Vitamin A acid, topical therapy was stopped and the patients were observed after Vitamin A acid withdrawal. If the clinical condition later deteriorated, Vitamin A acid was readministered. These investigations were performed over a year.

Nine patients who received 50 mg improved in 3 weeks, 25 at 10 mg improved by 6 weeks and 105 at 5 mg by an average of 7 months. Even after this successful long-term treatment, cessation of oral Vitamin A acid treatment sometimes brought a recurrence.

Ichthyosiform Dermatoses, Dyskeratoses
In comparison with acne vulgaris, the necessary dosage of Vitamin A acid for successful treatment of the anomalies of keratinization itself, such as ichthyosiform dermatoses, is considerably higher. In congenital ichthyosiform erythrodermia, we achieved improvement at 20 to 60 mg daily. After the initial improvement, the maintenance dose was 20 mg twice daily. Of 13 patients treated, showed side effects.

Darier’s Disease
These 8 patients needed high initial dose of 100 mg effects (cheilitis, rhinitis sicca, could be mitigated by palliat and early reduction to main levels. The dosage was reduced to 7 to 10 days by 20 mg. The maintenance dose was 20 mg twice daily. The smaller dose was often followed. Exacerbation, especially during the summer months, cease of the Vitamin A acid essay.

Pityriasis Rubra Pilaris
We treated 3 patients with significant improvement follo dosage of 60–80 mg twice a week for one week. 20 mg twice a week for a period of 3 months in improvement.

Psoriasis
After 24 to 48 hours the improvement was more evident. Further application caused the improvement in 50% of the treated within 1 month. After withdrawal, relapse occurred. Vitamin A acid can serve to results of cytotropic agents of treatment.

Skin Tumors
Our results were similar to Bollag’s in treating this condition, as oral application of higher doses of Vitamin A acid (50 to 100 mg) per regression per day of tumors and basal cell epitheliomas, an insensitivity to cytotropic agents observed. Our observation was extended to a 5-year follow-up; therapy alone is not recommended. Treatment for malignant tumors by successful oral treatment of basal cell epitheliomas, cell clusters of
Dieter’s Disease

These 8 patients needed a relatively high initial dose of 100 mg daily. Side effects (cheilitis, rhinitis sicca, skin cleavage) could be mitigated by palliative measures and early reduction to maintenance dose levels. The dosage was reduced at intervals of 7 to 10 days by 20 mg. The maintenance dose was 20 mg twice daily. A smaller dose was often followed by relapse. Exacerbation, especially observed during the summer months, made an increase of the Vitamin A acid dosage necessary.

Pityriasis Rubra Pilaris

We treated 3 patients who showed a significant improvement following initial dosage of 60–80 mg twice daily reached after one week. 20 mg twice daily given over a period of 3 months maintained the improvement.

Psoriasis

After 24 to 48 hours patients taking Vitamin A acid show increased scaling. Further application caused improvement of psoriasis in 50% of the 45 patients treated within 2 months. After drug withdrawal, relapse occurred. Oral use of Vitamin A acid can serve to improve the results of cytostatic agents or local treatment.

Skin Tumors

Our results were similar to those of Bollagö in treating this condition. After oral application of higher doses of Vitamin A acid (50 to 100 mg) and a slower regression per day of tumors such as basal cell epitheliomas, an increased sensitivity to cytostatic agents and X-rays was observed. Our observations have been extended to a 5-year follow-up. Oral therapy alone is not recommended as treatment for malignant tumors. In successful oral treatment of basal cell epitheliomas, cell clusters could also be observed histologically in deeper lying layers.

Leukoplakia

Therapy with Vitamin A acid was used initially by Desai in India, where patients’ mucous membranes are constantly stimulated by the chewing of betel nuts and other forms of irritation. Four to 8 weeks after an oral dosage of 50 mg, considerable improvement occurred.

In another series, a considerable improvement was reported with a dosage of 40–80 mg over a period of 3 months.

Lichen Planus

The same observation of successful treatment was made, with some exceptions, with lichen planus of mucous membrane. Eight patients were treated with an initial dosage of 60–80 mg. With one exception all patients showed a significant decrease of mucous membrane alteration within a treatment period of 8 weeks. Complete healing was not achieved, even over a 14-month observation period and with a dose of 20 mg twice daily. When Vitamin A acid therapy was stopped, the condition worsened.

Discussion

We assume that an increase in mitosis by Vitamin A acid mainly affected the differentiated cell types of the human skin and mucous membrane. The growth of undifferentiated cells was inhibited or their sensitivity toward other therapeutic measures was increased. It is likely that such opposing effects are responsible for the drug effect on keratosis. Vitamin A acid increases the dividing capacity of cells in the stratum germinativum, and at the same time, a cytology of nondividing differentiated cells occurs in the upper layer of the epidermis. The dyskeratic zone is removed, normal proliferation is stimulated and normal epidermal homeostasis re-established.
The successful treatment of dermatoses such as acne with comedones, ichthyosiform dermatoses and follicular dyskeratoses does not require irritation as part of healing.

This effect can be related to higher concentration of Vitamin A acid in the superficial layers of the skin. Such a high level of Vitamin A acid cannot be created by oral application because of its toxicity. The general side effects of oral therapy with 50–100 mg/day limit its application.

References


Tetracycline-Stained Teeth in Children

Most physicians recognize that exposure to tetracycline between the fifth month of fetal life and age 8 often results in discoloration and sometimes hypoplasia of permanent as well as deciduous teeth.

Recent NIH research indicates that the risk of tetracycline staining is particularly high during the first year of life because of the inability of immature kidneys to excrete these drugs efficiently.

Tetracycline discolaration results because the drugs have an affinity for calcifying tissue. During tooth formation, tetracyclines are incorporated chiefly into dentin. They may also interfere with enamel formation.

Front teeth normally have thin enamel coatings. Thus tetracycline-stained dentin is readily visible through damaged overlying enamel.

The tooth discolorations, ranging from yellow through brown to gray, usually result in acute embarrassment to young children. They sometimes lead to considerable psychological damage. — Research findings of potential value to the practitioner. JAMA, 237:636, 1977.

Sipple's Syndrome

A potentially important aj the study of the pathogenesis is to determine whether it is multiclonal cell origin. Gen- thought that tumors of monol- gin arise as a consequence matic mutations in a single tissue of origin. These must arise spontaneously or may be of viral or carcinogen transfor- Tumors of multiclonal or- through processes that af- cells in the target tissue, e carcinogens, a general sus- tissuc cells to malignant char normal response to hormon- or an excessive stimulative tissue cells. Most spontane- tumors in man have been fou a "clonal" or single cell o chronic myelocytic leukemia carcinoma of the colon, hav conal origin. Studies of 2 transmittted tumors in man, tri- llomas and neurofibromas, in they are of multiclonal origin.

Data supporting the monol- of hereditary tumors have not been reported. Baylin and studied a Negro woman wi