

RETINOIDS: NEW SKIN FOR THE OLD

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The retinoids have recently received considerable publicity in the lay press over the controversy of the teratogenic effects of the oral retinoids and the claims of anti-aging and anti-wrinkle effects of the topical tretinoin. Retinoids are derivatives and structural analogues of vitamin A (retinol). Vitamin A has long been known to dermatology to benefit disorders of keratinisation. The low therapeutic ratio and the resulting acute and chronic toxic effects of vitamin A limited its clinical use. The newer synthetic oral retinoids show a wider margin of efficacy to toxicity. The retinoids presently available for clinical use are:

1. Topical tretinoin — Retin A, Eudyna, AiroI
2. Oral isotretinoin — Roaccutane
3. Oral etretinate — Tigason

Retinoids modulate cellular proliferation and differentiation of epithelial cells via activation and simultaneous suppression of specific genes, affecting the appearance or repression of more than 40 specific proteins. They thus have a diversity of biologic effects in the skin which include regulation of epithelial differentiation, antineoplastic effects, increase collagen synthesis, enhanced wound healing, immunomodulation and anti-inflammatory effects.

Topical tretinoin was first used in disorders of keratinisation but did not gain acceptance because of skin irritation. Successful treatment of acne vulgaris with topical tretinoin in alcoholic solution was again slow to be accepted by dermatologists because of its associated irritant effect. The subsequent introduction of the cream and gel formulations with less potential for irritancy resulted in greater acceptance. Topical tretinoin exerts its effects in acne vulgaris by the normalisation of the abnormal desquamation of the follicular epithelium which is central in the pathogenesis of acne. In clinical terms, this is a comedolytic effect on both the open (blackheads) and the closed (whiteheads) comedones. New comedone formation is reduced. Topical tretinoin remains the mainstay of maintenance phase therapy of acne vulgaris.

Of recent times, topical tretinoin has a rebirth in its role as the well publicised "wonder anti-aging cream". In 1986 Kligman et al published a study on topical tretinoin in the treatment of photoaged skin in humans. He showed by elegant histologic studies that topical tretinoin is capable of partially reversing the structural damage (atrophic epidermis, epidermal dysplasia, actinic keratoses, collagen degeneration) of excessive sunlight exposure and

may be useful in decelerating the photoaging process. In addition they showed dispersion of previously clumped melanin granules and improved angiogenesis. More recently in 1988 Weiss et al from the University of Michigan showed clinical and histological improvement in photoaged skin in a double blind vehicle controlled study of 40 Caucasian patients with a mean age of 50 years (range 35-70). The patients applied the study compounds once nightly for 16 weeks. The clinical parameters most improved by the active medication were fine wrinkling, coarse wrinkling and roughness. A statistically significant improvement was seen on the tretinoin treated sites.

An enthusiastic response followed this report as it was picked up by the lay press and resulted in phenomenal sales of the product to a point of scarcity. As physicians it is important to maintain objectivity and present a balanced view on what tretinoin can and cannot do. Firstly tretinoin is not an anti-aging cream as claimed by the lay press. The medical profession has shown that tretinoin improves the appearance of photoaged skin. The lag and sagging folds is beyond the repair of tretinoin. Seborrhoeic keratoses and skin tags are also non-responsive. Solar induced freckles and lentigenes only show mild reduction in colour. Tretinoin did not improve telangiectasia. The poikilodermatous (chicken skin appearance) changes on the sides of the neck do not respond to tretinoin. The effects of tretinoin in pigmented aged skin (non caucasian) have not been studied. As for the permanence of the beneficial effects, it appears that long term or lifelong maintenance application 3 to 4 times a week would be necessary. Initial data seem to suggest that continued improvement may occur with long term (12 months) use, but further long term studies are needed.

Irritation is a common side effect and can lead to intolerable irritant contact dermatitis, needing treatment with topical steroids. This dermatitis may be exacerbated by exposure to heat, sweat and the sun, all of importance in our climate. Excessive drying and scaling is another side effect needing reduction in the usage and treatment with emollient. Transient stinging of the face and around the eyes are common. Patients also complain of a biting and pulling sensation when washing their face. Adequate patient instruction by the physicians in the proper use of topical tretinoin is essential to minimise the side effects.

Retinoids have been shown to eliminate dysplastic cells and small actinic keratoses. Medically this is a more important effect of topical tretinoin on photoaged skin. The potential for chemoprevention of premalignant lesions is exciting as we ourselves are facing an aging patient population. However physicians should educate the susceptible persons on the use of sunscreens and the avoidance of excessive exposure to sunlight and ultraviolet light in tanning saloons as important preventive measures to photoaging and skin cancers.

There is a message for physicians who persist to decry the cosmetic concerns of our patients as being an

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area too demeaning for the medical profession. To disregard the psychological benefits and the improvement of the person's self esteem and well being by improvement of the cutaneous appearance is revealing the physician's ignorance of the concept of total health. With the judicious use of tretinoin in the older person, the medical benefits on premalignant skin lesion can be combined with the patient's improvement of self esteem.

There is a message for the cosmetic industry which

has for years claimed, unchallenged, skin rejuvenation and anti-aging properties of their products like vitamin E, collagen creams, calf serum and the like. The challenge is now for the cosmetic industry to substantiate their claims by doing comparative studies with the new proven standard — topical tretinoin. The health authorities regulating advertisements should take the cue and prevent the continued onslaught of unproven claims and half truths on the general public.

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