Treatment of Photoaged Skin
Efficacy, Tolerability and Costs of Available Agents

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Summary

Photoaging is a cumulative degenerative process induced by solar irradiation with well defined clinical and histological correlates. Because of its huge psychological impact, there is much demand for effective treatment.

Many well constructed trials confirm the clinical efficacy of topical tretinoin for improving fine wrinkling and mild to moderate hyperpigmentation; coarse wrinkling and severe hyperpigmentation respond less well. Histological improvement is well documented, but the precise relationship to clinical response is not clearly established. Tolerability can be a problem. Optimal concentrations are not firmly established and vary between patients. Claims that topical isotretinoin is better tolerated than tretinoin need to be confirmed with well constructed trials.

Despite many claims, there have been no adequate trials documenting the efficacy of fish cartilage polysaccharide extracts or α-hydroxy acids.

Careful patient selection with consideration of alternative treatments such as chemical peeling, dermabrasion and surgery is important to successful management of photoaging.

Photoaging consists of cumulative changes in the skin caused by exposure to solar ultraviolet radiation over a number of decades. There is marked loss of elasticity with the development of fine and coarse wrinkles. The skin surface becomes dry with a yellow hue and the melanin pigmentation often becomes mottled. Telangiectasias and a variety of neoplastic growths (many premalignant) develop.[1,2]

These observed changes can be correlated to a series of pathological changes including epidermal atrophy with an accumulation of elastic fibres and an amorphous elastotic material in the dermis. This is in contrast to true chronological aging of the skin in which there is loss of elastic fibres.[3] Patients nevertheless equate photoaging changes with chronological aging, so that there is considerable psychological impact.[4]

There is a huge demand for agents that might
correct the changes of photoaging. This article will attempt to review some of the more well-known agents, examining their efficacy, tolerability and costs.

1. Tretinoin

1.1 Efficacy

The vast bulk of the scientific literature regarding the pharmacological treatment of photoaging relates to topical tretinoin. Tretinoin is all-trans retinoic acid, a derivative of vitamin A, or a retinoid. It has long been known that tretinoin has effects on disorders of epidermal keratinisation, such as ichthyosis and acne. In 1962, Stuttgen first alluded to the efficacy of tretinoin for treating sun-induced lesions such as actinic keratoses. Over the next decade it became apparent that retinoids, both topical and oral, had a profound effect on many dermatological conditions.

Kligman et al. used a hairless mouse model to demonstrate that tretinoin could reverse histological changes induced by chronic UVB-radiation exposure. This effect was dose-dependent and could not be duplicated using a number of irritants suggesting a true pharmacological rather than contact irritant effect.

Based on this study and observations of the effects of tretinoin on coincidental photoaging in acne patients aged 30 to 50 years, Kligman conducted the first human study into the effects of tretinoin on photoaging. In this open placebo-controlled study, biopsies were performed before and after application of tretinoin 0.05% cream daily for 3 months. Kligman has suggested that histological signs of photodamage may predate clinical signs by decades. Indeed, in patients with clinically mild damage, there was marked histological improvement although clinical benefit was less obvious than in those patients with clinically severe photodamage.

Many clinical studies have confirmed and extended these findings. Weiss et al. showed clinical and histological improvement in 93% of 15 patients using 0.1% tretinoin on the face and 100% of 30 patients treating the arms in a 16-week double-blind placebo-controlled study; patients were White and had mild to moderate photodamage. In a large double-blind multicentre study of 251 patients, Weinstein et al. compared different strengths of tretinoin, finding a 79% improvement with 0.05% cream compared to 57% for 0.01% cream, and 48% for vehicle alone according to both clinical (fine wrinkling, hyperpigmentation, rough texture and skin laxity) and histological factors (increased epidermal thickness and decreased melanin content). The improvement seen in the control group probably reflects the benefit from the concurrent use of sunscreens and emollients allowed in this study.

Similar results were obtained from another large multicentre study by Olsen et al. of 296 White patients with mild to moderate photodamage (patients with severe photodamage were excluded). 68% improvement was seen in those patients using tretinoin 0.05% cream, but no significant difference between 0.01% and 0.001% creams and vehicle (43% improvement).

Studies on Japanese and Thai patients indicate efficacy is not confined to Caucasian skin. Griffiths et al. have shown improvement in the hyperpigmented lesions that form a predominant component of photoaging in Chinese and Japanese patients. Pigmentary changes such as solar lentigines and freckles also improved. Rafal et al. have shown similar clinical and histological improvement in solar lentigines. To avoid subjectivity of clinical assessment, Grove et al. used digital image analysis confirming the improvement in wrinkling and skin texture changes.

Tretinoin is unable to correct severe photoaging changes such as deep wrinkles and marked cutaneous laxity even after continuous use for 6 years. However, histological improvement is maintained. Ellis et al. reported sustained benefit from continued therapy for up to 22 months.

Tretinoin is not effective for deep wrinkles and is less reliably effective for very dark hyperpigmentation.