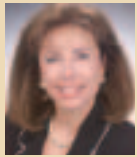




Clinical Insights

Optimizing Topical Tretinoin Therapy for Cutaneous Aging



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Over the past several years, as the Baby Boomers have entered mid-life, the demand for cosmetic dermatology procedures and services has grown steadily—and so has the number of available treatment options. As more aesthetic interventions have emerged, younger patients in their thirties and early forties have become increasingly interested in treatments that may halt or reverse cutaneous aging. Across this continuum of patients from relatively young to elderly, no aesthetic product or service offers the broad application of topical tretinoin. A true cornerstone of aesthetic dermatology, topical tretinoin is a reliable and proven anti-aging therapy that works well on its own or in combination with other interventions to reverse skin aging.

Skin Aging and Tretinoin

The effects of solar radiation on the skin have been well studied. In addition to the risk for melanoma and non-melanoma skin cancer, chronic UV exposure is associated with UV-induced photoaging, characterized by leathery texture, wrinkles, laxity, and sallowness. These manifestations of photoaging have been largely attributed to UV induction of matrix metalloproteinases (MMP) that degrade collagen.¹ In addition to its detrimental effects on connective tissues, UV exposure is linked to the development of senile lentigines² and activation of melanocytes, resulting in mottled hyperpigmentation.³

Dermatologists have long asserted that the ideal method for dealing with the negative effects of UV radiation on the skin are to avoid them in the first place. Hence, patients are advised to wear sunscreen daily and to limit exposure to UV radiation as much as possible.⁴ Yet even the most ardent sun-avoider is exposed to UV radiation. Even if one could fully avoid photo-damage, natural skin aging would nonetheless take place, marked by changes in muscle, bone, fat, and skin structures.⁵

Therefore, treatment aimed at reversing the effects of chronic UV exposure and chronological aging is necessary. Of the numerous topical anti-aging products on the market, none has as much research to support its use as tretinoin does. Tretinoin is shown to thin the stratum corneum and thicken the

epidermis, reversing changes that naturally take place in the skin with advancing age.⁶ Additionally, tretinoin therapy initiates new collagen formation⁶ apparently via increased production of procollagen⁷ and prevents further skin aging by inhibiting UV-induced production of MMPs.

Data support the efficacy of tretinoin monotherapy for treatment of hyperpigmentation and lentigines.⁸ Topical retinoids decrease melanosome transfer and inhibit UV-B stimulated tyrosinase activity and melanin synthesis.⁹

Given its multiple activities and its ability to stop and reverse UV-induced and chronological skin aging, topical tretinoin is the quintessential gold standard for topical antiaging therapy. Unlike topical antioxidants, which work primarily to prevent free-radical induced skin damage and aging, topical tretinoin actually repairs damage caused by sun exposure and natural aging. Topical tretinoin reverses skin aging while these other agents simply try to prevent it.

Optimizing Treatment

Despite its remarkable utility, topical tretinoin is associated with some degree of irritation, particularly during the initiation of therapy. Patients may experience cutaneous irritation and erythema (there was even early speculation—since disproven—that antiaging effects of tretinoin are initiated as a response to irritation¹⁰). For certain patients with very fair, sensitive skin, topical tretinoin can be particularly irritating; a few patients may only tolerate retinol-based (a tretinoin pro-drug) agents to initiate therapy. Most patients, however, can tolerate topical tretinoin when an appropriate formulation is introduced on a “titration” schedule. Patients can be instructed to initiate treatment with application every third night and gradually increase to nightly application as they feel comfortable. Given the way that tretinoin works to prevent and repair cutaneous aging, patients should anticipate using the agent every day indefinitely; therefore, there is no need to rush into therapy. With time, patients become tachyphylactic to the irritating and drying effects of tretinoin.

In my practice, I have found that patients experience increased comfort and tolerability when using topical tretinoin emollient cream 0.05% (Refissa, Coria Laboratories), which provides hydrating effects. The thick, unscented, hydrating base obviates the need for concomitant application of a moisturizer, a common tolerability-enhancing tactic used with other tretinoin formulations. Of course, patients may apply addition-

Tretinoin Treatment Pearls

Important treatment areas are the décolleté and the hands. In the décolleté area, chronic sun exposure often leads to uneven pigmentation and a crepey appearance of the skin. By evening skin tone and thickening the epidermis, topical tretinoin 0.05% can reverse the signs of aging on the chest. Similarly, for the hands, the benefit of epidermal thickening is especially important to provide a more youthful appearance.

Topical tretinoin may also be useful to combat Bateman's actinic purpura.¹⁴ With age, the skin of the forearms changes: the epidermis thins and the stratum corneum thickens. This aged skin is more susceptible to injury and prone to development of purpura. Of course, anticoagulant therapy also increases the risk for purpura in the elderly population. Application of topical tretinoin to the forearms can actually help to thicken the epidermis and thin the stratum corneum, returning the skin to a more natural function and reducing the risk of purpura.

al moisturizer at any time to increase compliance.

With its 0.05% concentration of tretinoin, Refissa is the strongest tretinoin formulation on the market for treatment of photoaging.

Patients do best initiating and maintaining topical tretinoin therapy when they have realistic expectations. As noted, patients should titrate therapy gradually, and they should be prepared to develop some degree of irritation. Patients should also understand that daily use of a sunscreen SPF 15 (preferably 30) or higher every day is mandatory—otherwise they risk undoing the beneficial effects of tretinoin therapy.

Advise patients that once they start using topical tretinoin, they will continue using it for the rest of their lives. One potential oversight on the part of clinicians is to dispense too little topical tretinoin to the patient. Given the long-term nature of the therapy, writing for a 40g or 60g tube of tretinoin emollient cream is a good way to encourage compliance.

Given that topical tretinoin for rejuvenation is associated with out-of-pocket costs for patients, prescribers may be advised to weigh therapeutic costs and discuss treatment options with patients. Of note, a review of drug costs at one reputable online US pharmacy revealed that a 40g tube of Refissa cost just \$10 more than generic tretinoin 0.05% cream.¹¹

An Important Adjunct

Topical tretinoin monotherapy, a safe and effective treatment for photoaging, is particularly beneficial for patients with early signs of skin aging, including the patient in her (or his) thirties or forties. It can also be an important adjunct to other aesthetic interventions for more significant aging.

The use of topical tretinoin in conjunction with dermal fillers is an ideal approach to comprehensive rejuvenation. Dermal fillers replace volume lost with time and help to reduce the appearance of moderate to deep wrinkles. However, fillers do nothing to improve surface texture and tone. It seems that cosmetic dermatologists have only recently acknowledged the need to use topical interventions synergistically with dermal fillers to improve skin texture and tone. For patients with more advanced aging, chemical peels with salicylic acid or Jessner's solution are beneficial and may provide an exfoliative effect

that can enhance the penetration of topically applied tretinoin. For filler patients with milder wrinkling and mottled hyperpigmentation, topical tretinoin alone may be appropriate. In either case, all patients treated with fillers should use sunscreen and topical tretinoin as a long-term maintenance therapy to optimize anti-aging effects, treat fine lines and wrinkles, and help maintain a younger skin appearance.

A unique feature of Refissa is that it is indicated for the treatment of hyperpigmentation. This is an important clinical benefit, as hyperpigmentation is a common concern among patients. Importantly, however, research shows that the appearance of hyperpigmentation or uneven skin color increases an individual's apparent age significantly and, along with wrinkling, is one of the primary contributors to perception of advanced age.^{12,13} Improvement of hyperpigmentation can reduce an individual's perceived age by several years to as much as a decade.

The Quintessential Gold Standard

The only topical agent proven to reverse the effects of skin aging, topical tretinoin should be a part of the treatment algorithm for any patient interested in rejuvenation. Whether used as monotherapy or in conjunction with more advanced aesthetic procedures, tretinoin has a proven track record of safety and efficacy. Outcomes and compliance are optimized when patients are properly educated about the goals of therapy, possible side-effects, and the need for long-term therapy. In clinical practice, use of an emollient formulation of tretinoin 0.05% is associated with good tolerability and patient satisfaction. ●

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