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Background

Cosmetic procedures that restore lost volume and relax muscles allow cosmetic surgeons to reverse several cardinal signs of an aging face. However, the reversal of these symptoms does nothing to restore the epidermis to a more youthful appearance. Fortunately, there are treatments ranging from laser resurfacing to chemical peels to cosmeceuticals to topical retinoids to accomplish this goal. As surgical and nonsurgical procedures have improved, there has been a significant increase in their popularity. This increased popularity has been paralleled by improvements in retinoid technology. Retinoids have become an important component of many aesthetic treatment regimes, and it behooves all cosmetic physicians to have an understanding of their roles.

Topical retinoids have been used in dermatology for decades following the first report of their use for cosmetic indications by Kligman et al. (1986). In the decades since their introduction, they have gradually been adopted by all aesthetic

specialties. Since their original formulation, there have been multiple improvements in the vehicle that delivers tretinoin as well as modifications of the original molecule. Originally approved for the treatment of acne, retinoids were subsequently noted to reverse fine lines and wrinkles. Microscopically, these drugs demonstrate a remarkable ability to restore the dermis and epidermis to a more organized, thickened appearance. After several months of treatment, collagen fibers became more organized and youthful appearing (Griffiths et al. 1993). Clinical trials performed with tretinoin applied for several months were notable for significant reductions of lentigines and other stigmata of aging (Gilchrest 1997). Additional benefit stems from improvement of keratinocyte organization. Histologic analysis from periorbital skin treated with .02 % tretinoin demonstrated improvement of both collagen and elastin fibers (Kircik 2012). Based upon these findings, the author concludes that .02 % tretinoin is a reasonable treatment for the treatment of photoaging. As such, retinoids are a rational addition to any cosmetic treatment or regimen.

Derived from retinol (a vitamin A derivative), these compounds vary in the degree of oxidation as well as the chemical structures added to the parent compound. Retinol is converted to all-trans-retinoic acid (tretinoin) by the body, and the latter compound is 20-fold less effective than tretinoin. A second retinoid used for cosmetic indications is tazarotene. Tazarotene has been

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shown to be at least as effective as tretinoin for remodeling of the epidermis and dermis (Kang et al. 2001). At the present time, this molecule has been marketed as a treatment for acne and psoriasis as well as photorejuvenation. One drawback to its use is the high rate of irritancy. Modification of the dosing regimen to every other day or every third day for a period of about 6–8 weeks may help to decrease irritancy. Adapalene, another of the topical retinoids, has gained acceptance as a topical treatment for mild to moderate acne. To date it has not been formulated in a vehicle that is optimal for cosmetic indications, but patients sometimes combine it with a moisturizer.

Tretinoin originally had a concentration of 0.025 %. Later generations increased this to 0.05 and 0.1 %. In addition, emollient vehicles and “microsponge” technology have been employed to enhance tolerability of the product and increase patient compliance. One compound popular for its antiaging effects is the 0.05 % tretinoin emollient cream Renova. When used for several months, this product produces a skin that appears more youthful histologically as well as clinically. The role of the retinoids for cosmetic indications is expanding rapidly. Clinicians now routinely incorporate these products into their topical treatment regimens. They may be used with nonprescription cosmeceuticals such as glycolic acids, green tea, growth factors, vitamin C, and a host of other products. The optimal skin care regimen incorporating retinoids with these products has yet to be defined and most likely requires some trial and error based on the skin type of the individual being treated. Newer iterations of the molecule include tretinoin cyclodextrin complex which is a formulation designed to decrease irritancy. This molecule encapsulates the tretinoin molecule in an oligosaccharide shell. Clinical trials with this compound have demonstrated that it not only has equal efficacy to tretinoin but also that the combination decreases irritancy and thus enables better compliance (Miura et al. 2012). Future combinations may increase the percentage of tretinoin and thereby improve clinical and histologic improvements.

As with other products, there has been a rise in the importation of retinoid products with the

result that some of what patients use is not an FDA-approved product. It is likely that a fair amount of products that are imported may be counterfeit as is the case with many other drugs. Patients should be made aware of this possibility.

Retinoids also have a place as adjunctive therapy to “prime” the skin. Treatments using chemical peels, lasers, intense pulsed light, and perhaps even poly-l-lactic acid may be affected by the degree to which the epidermis and dermis have been pretreated with retinoids. In particular, pretreatment prior to use of 1927 laser, intense pulsed light, or CO₂ laser in patients that are type III or higher may benefit from inclusion of a retinoid in conjunction or in lieu of a hydroquinone. A clinical trial comparing fractional erbium resurfacing, intense pulsed light, tretinoin therapy, and nutritional supplements using amino acids demonstrated statistically significant improvements in wrinkle area and skin elasticity with all treatments administered (Ooe et al. 2013). Interestingly, this study found that patients in each arm thought that the treatments improved their skin to the same degree. This begs the question of whether combinations of these treatments would be synergistic and if so, what sequence and dose are optimal. Retinoids have been combined with a variety of other products and procedures to enhance patient outcomes. The use of tretinoin .05 % cream with 4 % hydroquinone in patients undergoing injections of type A botulinum toxin to the upper face yielded significantly greater improvements in the fine lines as well as the pigment of treated subjects (Schlessinger et al. 2011).

Retinaldehyde 0.05 % has been shown to improve outcomes of nonablative laser treatments (Mordon et al. 2004). Recently, retinaldehyde has been shown to potentially depigment the skin by decreasing melanin concentration rather than by exerting a cytotoxic effect on melanocytes (Sorg et al. 2013). This quality is likely to be helpful for clinicians seeking to avoid the use of hydroquinones because of concerns regarding their safety. Vitamin A palmitate in an oil-based vehicle demonstrated an ability to improve photodamage and improve the texture of the skin (Rawlings et al. 2013).

Retinol has been added to a wide range of products ranging from the most affordable to the most expensive. One clinical trial of a very affordable 0.1 % retinol cream showed an improvement of fine lines, wrinkles, and pigment after 8 weeks (Tucker-Samaras et al. 2009). A stronger, 1 % topical retinol cream in a novel formulation was demonstrated to improve photo-damage to a greater degree than did the 0.5 % concentration of the same product (Gold et al. 2013). However, the lower concentration was shown to be less irritating. It is likely that as better vehicles are formulated and additional ingredients added, the concentrations of retinol will be increased. More studies of this type need to be performed to discover whether treatment with retinoids improves surgical outcome with various cosmetic procedures.

Quite simply, almost all cosmetic patients should be using retinoids. Patients who are irritated by the use of these products should use low concentrations of them or apply them twice per week until they are able to tolerate stronger or more frequent applications. The use of retinol or one of the other retinoids available without a prescription is beneficial from a variety of cosmetic perspectives.

In clinical practice, the most commonly used retinoid for cosmetic indications is tretinoin. Many patients begin with the 0.025 % cream. Whenever possible, many use the Retin A brand of tretinoin because of the degree of comfort with the vehicles used for the family of products as well as the consistency of the product. For patients with oily skin, many physicians will use Tazorac or Retin A gel instead of Retin A cream. Different outcomes using the same strength may result because generic products may not always be from the same manufacturer. This may result in varying concentrations and vehicles, which can affect patient compliance. Newer retinoid products have been packaged with cleansers and moisturizers and sold as a packaged prescription product. This packaging was largely an attempt to supply patients with a retinoid that could not be substituted by a generic.

For patients who are Fitzpatrick type I or II, it is reasonable to apply the cream every other night. They are instructed to apply the cream to

dry skin, as applying it to moist or wet skin may increase the risk of irritation. After approximately 6–8 weeks, they are instructed to try to increase the application to nightly. If the skin becomes irritated, they are told to continue every other night usage for another 6–8 weeks before trying to increase the frequency again. Some patients simply will not tolerate the daily usage of retinoids, and for these individuals, it is reasonable to switch them to another product such as a retinol, vitamin C, or a growth factor-containing product on their “off” nights. This ensures that the patient is using something nightly (which increases compliance) as well as provides the patient with the benefits derived from using another cosmeceutical. One can vary the cosmeceutical used based on the patient’s goals, skin type, budget, and experience in the past. Many patients use various antioxidant products with retinoids, and there may be a synergistic effect with some ingredients.

Patients who tolerate the 0.025 % tretinoin cream for 3 months may progress to the 0.05 cream. As patients tolerate this, increase the concentration that they use. For most patients, the 0.05 % cream is as high as they can tolerate, although some patients, particularly those with type III or IV skin, can go to the 0.1 %. Several patients who have used retinoids for decades have graduated to the 0.1 %. Interestingly, they report very little irritation and minimal photosensitization.

The use of retinoids in skin of color remains an understudied area. However, there is evidence that retinoids may be safely used in skin of color and that they may decrease postinflammatory hyperpigmentation. Many clinicians avoid the use of retinoids for patients with skin of color because of concern about the inflammatory potential of these molecules. However, judicious use of these molecules in skin of color can improve the hyperpigmentation rather than exacerbate it (Woolery-Lloyd et al. 2013).

Microsponge technology and an emollient base are variants of the basic tretinoin formula. Adding the emollient makes the product slightly less irritating, and it has a role for a select few patients. The microsponge technology delivers the active ingredient more efficiently. In practice,

it is easier and less expensive to maximize the concentration of the traditional formula before migrating to the more expensive micro sponge.

Tazarotene is available as a cream, gel, and as a foam formulation. This product will restore the epidermis and dermis to a more youthful appearance clinically and histologically. It does not seem to have the patient acceptance of Retin A and may be slightly more irritating.

As previously mentioned, many cosmetic patients will benefit from pretreatment with retinoids. Patients undergoing nonablative laser, intense pulsed light, and perhaps injections of poly-l-lactic acid should benefit from treatment with retinoids. For patients undergoing nonablative laser or intense pulsed light, treatment with the 0.025 % concentration should be utilized for at least 6 or 8 weeks to maximize outcomes. In theory, the inhibition of metalloproteinases caused by treatment with tretinoin should increase the collagen formation with injection of poly-l-lactic acid. To date, there are no studies to demonstrate that this is the case, but from a theoretical perspective, treatment with tretinoin for 6–8 weeks prior to injections as well as throughout the course of the treatment makes sense.

In conclusion, most cosmetic patients can benefit from the use of retinoids. They are great adjuncts for rejuvenation and potentially may increase the utility of various cosmetic procedures performed. Tretinoin has the longest record of safety and efficacy in this category, but other products are available, and more are on the horizon.

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