COMPLEMENTARY EFFECTS
OF TOPICAL ANTIAGING TREATMENTS
IN CONJUNCTION WITH AESTHETIC PROCEDURES

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Abstract
The dermatologist has a variety of tools for improving the appearance of aging skin. These include injectable botulinum toxins and dermal fillers, laser treatments, chemical peels, and various topical agents, including cosmeceuticals. A combined approach using more than one facial rejuvenation tool is considered ideal for many patients, as it targets the various areas of the face and numerous dynamic and static changes associated with aging. A topical cosmeceutical regimen, such as one containing tretinoin and hydroquinone, can enhance the effects of facial rejuvenation procedures and encourage patients to adopt a daily cleansing and rejuvenation regimen that they can continue after the procedure to help maintain the aesthetic effects.

Introduction
Aging of the face involves both dynamic and static changes in the skin, musculature, bone, and fat, and the dermatologist has numerous tools to assist patients in enhancing facial appearance (Table 1). Given that virtually all of the aging changes are multifactorial in origin, a combined approach is considered ideal for many patients. Patients’ concerns regarding their aging are not usually related to one particular area, but rather the aging face in general. Treatment can be individualized and directed toward the most pronounced changes, which are unique to each person. Furthermore, use of multiple treatments may prolong responses and prevent further changes, particularly when the combination includes a topical regimen.

Benefits of Combining Aesthetic Procedures
Although it is intuitive that combination treatments will yield better results than a single aesthetic procedure, several studies have attempted to quantify these benefits. In a study in which 38 subjects were randomized to receive botulinum neurotoxin type A (BoNTA) plus hyaluronic acid (HA) versus HA alone for moderate-to-severe glabellar lines, not only was there a greater aesthetic effect with a combination versus a single-product treatment at measured time points, but the longevity of treatment was substantially prolonged with combination treatment. The median time to return to preinjection glabellar furrows was 32 weeks with BoNTA plus HA versus 18 weeks with HA alone.1 In another recently presented analysis of pooled data from 6 clinical studies, Carruthers et al2 observed that a larger proportion of patients (62%) reported looking younger following BoNTA treatment of multiple upper facial areas (glabella, forehead, and crow’s feet) than did patients receiving BoNTA for single areas of the face (crow’s feet, 45%; or glabella, 40%). Thus, the multiple treatment produced a greater benefit in terms of self-perceived youthfulness.

Carruthers and Carruthers1 compared the results of full-face broadband light (BBL) with that of full-face BBL combined with BoNTA treatment of moderate-to-severe crow’s feet in 30 female subjects. While BBL alone produced remarkable improvements in telangiectasias, lentigines, and skin texture, the BoNTA cotreatment increased these results by 15%. These observations led the investigators to postulate a possible synergistic, as well as complementary, effect.

Topical retinoid and/or hydroquinone regimens have been used prior to ablative and nonablative skin resurfacing procedures for many years.3 In a survey of 339 dermatologists and plastic surgeons performing laser resurfacing, retinoin was recommended for pretreatment skin care by 80% of respondents, and hydroquinone was recommended by 69%.

Table 1. The toolbox for nonsurgical facial rejuvenation.

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<td>Dermal fillers:</td>
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a comparative study among 40 Indian women with melasma, the combination of a modified Kligman's cream formula (tretinoin 0.05%, hydroquinone 5%, and hydrocortisone 1%) plus glycolic acid peels was significantly more effective in improving melasma than was with a modified Kligman's formula alone. For treating acquired dermal melanocytosis with Q-switched ruby laser, pretreatment with tretinoin 0.1% and hydroquinone 5% was associated with lower rates of postinflammatory hyperpigmentation compared with earlier experiences with laser alone.

The adjunctive use of topical tretinoin and hydroquinone preparations may be beneficial with other types of facial rejuvenation procedures. A recently completed large-scale experience trial evaluated the combined effect of facial rejuvenation procedures with maintenance use of a 4-step proprietary skin care regimen containing 0.1% tretinoin and 4% hydroquinone as active ingredients along with a cleanser, toner, exfoliant, sunscreen, and moisturizer. This 4-step system has been previously shown to be superior to regimens containing tretinoin 0.1% cream plus over-the-counter (OTC) products, hydroquinone plus OTC products, and OTC products alone in terms of improving attributes of photodamaged skin such as periorcular and perioral fine wrinkles, mottled hyperpigmentation, clarity, sallowness, laxity, and tactile roughness.

In this recent study, 2697 patients from numerous study centers across the US who received various procedures such as BoNTA, dermal filler injections, laser treatment, microdermabrasion, chemical peels, or ablative surgery (lasers or facelift) also applied the 4-step tretinoin/hydroquinone treatment system for a mean of 4 weeks preprocedure and 6 weeks postprocedure. Patient demographics were typical of those who comprise the antiaging target market: 95% were female, 76% were between 35 and 65 years of age, and 89% had Fitzpatrick skin types II to IV. Approximately half of patients underwent ablative procedures, and half underwent nonablative, nonsurgical procedures. Physicians evaluated various attributes of skin quality of patients using a 4-point scale (0 = none to 3 = severe/prominent) before and after patients used the hydroquinone/tretinoin system in conjunction with a facial rejuvenation procedure. As expected, patients exhibited an improvement in skin texture attributes such as fine wrinkles, sallowness, tactile roughness, and hyperpigmentation (Figure 1). Results were similar among patients who underwent ablative and nonablative treatments.

Among patients who received BoNTA and the tretinoin/hydroquinone-based system (n=239), improvements of at least 1 grade in sallowness, tactile roughness, hyperpigmentation, and fine periorcular wrinkles were observed in ≥ 80% of patients (Figure 2). Thus, for patients seeking wrinkle reduction with BoNTA treatment, the complementary use of a tretinoin/hydroquinone-based treatment system is an effective adjunct, as it results in an additional improvement across multiple parameters of skin quality that would not be attributable to BoNTA alone.

**Optimizing Combined Antiaging Regimens**

**Preprocedure**

The use of a tretinoin/hydroquinone-based system may produce several benefits when used to prepare the skin prior to chemical peels, microdermabrasion, and nonablative and ablative laser treatments. Retinoids thin the stratum corneum, allowing for better penetration of laser light and

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**Figure 1.** Percentage of patients exhibiting at least a 1-grade improvement on a 4-point scale (0 = none to 3 = prominent/severe) in skin attributes following the use of a 4-step tretinoin 0.1%/hydroquinone 4%-based skin care system in conjunction with facial rejuvenation procedures.
agents such as aminolevulinic acid, if used. Pretreatment with retinoids prior to dermabrasion, deep chemical peeling, or laser resurfacing can accelerate re-epithelialization. It has been suggested that pretreatment with hydroquinone may suppress the production of new melanin and accelerate the return of skin to normal pigment should postprocedure hyperpigmentation occur. The lightening of background skin color with tretinoin and hydroquinone allows for the safer and more aggressive use of higher energy treatment parameters. This may be especially useful when treating the chest, hands, or arms with intense pulsed light (IPL), as these areas tend to have greater degrees of actinic bronzing than the face. If the same light setting is used on the chest/hands/arms as the face, there is a greater risk of burning the chest/neck/arms due to the increased melanin in these areas. An additional advantage regarding the use of any cosmeceutical pretreatment is that patients begin observing a daily cleansing and rejuvenation regimen that, it is hoped, the patient will continue after the procedure.

Given that many of the actions that have been documented with tretinoin (ie, reinvigoration of cellular function, enhanced collagen synthesis, reduced expression of matrix metalloproteinases, normalization of follicular keratinization, and enhanced wound healing) are similar to those sought with use of laser and light therapies, it seems prudent to initiate treatment with topical preparations like tretinoin and hydroquinone to jump-start these targeted processes in patients for whom laser or light treatments are planned. In some cases, topical treatment may obviate the need for laser resurfacing. Indeed, results have been obtained with a topical tretinoin/hydroquinone-based skin care system that are arguably similar to those that can be expected from a laser or IPL treatment (Figures 3 and 4).

In general, treatment with a tretinoin/hydroquinone-based system should be discontinued several days to weeks prior to microdermabrasions, chemical peels, and fractionated resurfacing. Discontinuation of pretreatment is not necessary prior to IPL or pulsed dye therapy; a more robust reaction is often observed when using topical pretreatment prior to photodynamic therapy due to increased absorption of the aminolevulinic acid.

**Postprocedure**

Patients can be instructed to reinitiate the topical tretinoin/hydroquinone-based regimen at their own discretion, when they feel both the procedure-related skin irritation and sensitivity have subsided. For patients in whom a series of procedures is planned (ie, chemical peels, photodynamic therapy, or fractionated resurfacing), it may be best to wait until the series is complete before reinitiating a topical cosmeceutical regimen. Once tolerated, topical cosmeceutical regimens can be continued indefinitely.

**Barriers to Use**

The 2 most common barriers to using topical antiaging products are local irritation induced by both retinoids and hydroquinone, and lack of patient motivation. In an open-label trial in which 120 patients with moderate-to-severe photodamaged facial skin received tretinoin cream 0.02% for 52 weeks, skin irritation (erythema, peeling, burning/stinging) was reported as an adverse event by 43% of patients. Most cases were mild to moderate, and only 6% discontinued therapy as a result. Irritation tended to peak during the first 2 weeks of tretinoin therapy, and skin sensitivity returned to baseline by week 8. Among patients who had previously administered the tretinoin 0.02% cream for 24 weeks, then stopped for 12 weeks and restarted therapy, irritation peaked later (4 weeks) during tretinoin restart, but also returned to

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Figure 2. Percentage of patients exhibiting at least a 1-grade improvement on a 4-point scale (0=none to 3=prominent/severe) in skin attributes following the use of a 4-step tretinoin 0.1%/hydroquinone 4%-based skin care system in conjunction with botulinum neurotoxin type A for facial rejuvenation.
baseline by week 8. Thus, tretinoin-naive patients and tretinoin restarters should be advised that skin irritation (e.g., erythema and dryness) can be expected to subside within 2 months of treatment initiation.

Some of the more practical means for attaining patient compliance with topical rejuvenation programs focus on proper patient education. For example, if the dermatologist and his or her staff are enthusiastic about the products and the results obtained, patients will be more likely to be motivated to try them. In our practice new patients are shown serial photographs from the practice’s own patient base showing improvements over time, and these are routinely reviewed with practice staff so they are familiar with them. Thorough explanations should be provided on how to use the products, what to expect in terms of results, and how to manage any irritation; these instructions also should be given in written format to reinforce verbal discussions. Last, serial photography is invaluable for showing patients how their skin has improved over time and can be a powerful motivation to continue to use the regimen. Patients will appreciate the extra care and interest shown them through the use of serial photographs. Staff members should be trained to point out specific areas of improvement that may not be immediately noticeable to the untrained eye. This is particularly important because results often occur gradually, so patients may not notice subtle improvements, especially in the first few weeks of treatment. Indeed, in a 24-week, double-blind, randomized, placebo-controlled trial evaluating once-daily application of tretinoin 0.02% cream,13 patient self-assessment scores of individual features of photodamage (small wrinkles, tone, color, texture, tightness, and pores) and overall appearance at 24 weeks were similar in the treatment group and the vehicle group, even though investigator assessments demonstrated statistically significant improvements in the tretinoin arm. These results are of interest given that noticeable improvements would be expected and did occur according to blinded-investigator assessments by 6 months, yet the patients did not perceive them. At 24 weeks, 62% of patients receiving tretinoin and 57% receiving the vehicle reported overall improvement (P = .34). However, patients’ perceptions of improvements changed in the long-term follow-up study, in which 77% of patients receiving tretinoin 0.02% cream for 52 weeks reported improvement.13

Summary

Topical antiaging regimens are an essential component of a comprehensive approach to skin rejuvenation. From a practice-building perspective, successful results with skin rejuvenation procedures offer several advantages (Table 2). All patients who seek aesthetic advice should be urged to initiate and maintain a daily topical rejuvenation program. Proper education of office staff and patients is a key component to attainment of the best results and highest possible levels of patient satisfaction with proven regimens.

Table 2. How does a dermatologic practice benefit from offering effective skin rejuvenation regimens?

| Builds trust and credibility when regimens are recommended that deliver great results. |
| Increases referrals when patients tell their friends about their great results. |
| Offers opportunities for patients to come back to the practice. |
| Helps patients advance to trying procedure-based solutions to their skin-aging problems in addition to topical treatments. |

References

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