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NOVEL TREATMENT SOLUTION

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Eskata (40% Hydrogen Peroxide Solution) for the Treatment of Seborrheic Keratoses

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“Barnacles,” “liverspots,” “age spots”: Seborrheic keratoses (SKs) have many different names, sizes, and clinical presentations in our patients. The only commonality among SKs is that patients despise them. While patients are initially concerned about their malignant potential, once they are reassured, most patients quickly transition from relief to request: “*Can you get rid of them?*” An observational study conducted across multiple dermatology practices found that SKs have a significant impact on quality of life, causing patients to adopt strategies to cover them and seek treatment for asymptomatic lesions.¹ Given their benign potential, the only reason to remove an asymptomatic raised SK is cosmetic. When doing a cosmetic procedure, the acceptable risk is often lower given that the benefit for treatment is aesthetic. Ideally, a cosmetic intervention would have a wealth of evidence-based data and a favorable side effect profile. Eskata 40% hydrogen peroxide topical solution, the only FDA-approved drug for the treatment of raised SKs, strikes the perfect balance between efficacy and side effect profile.

When topically applied to SKs, the supraphysiologic concentration of hydrogen peroxide in Eskata overcomes the antioxidant defense systems leading to the generation of reactive oxygen species, direct oxidative damage, and eventually apoptosis. Its efficacy was highlighted in two randomized, placebo-controlled trials that compared the safety and efficacy of 40% hydrogen peroxide topical solution for the treatment of SKs.² The two trials included 937 patients with 4 SKs who were randomized 1:1 to Eskata or vehicle. At day 106, significantly more Eskata patients achieved complete clearance on all 4 SKs (4% or 8% vs 0%) and 3 of 4 SKs (13% or 23% vs 0%). A post-hoc analysis found the clearance for SKs was higher for the face than other body sites (65% for face versus 46% for trunk and 38% for extremities). Dyspigmentation rates were also lowest among SKs treated on the face.³ The high response rates with low side effect profile for Eskata treatments on facial SKs are very important given how cosmetically concerning facial lesions tend to be for patients.

Before the FDA approval of Eskata, traditional treatment options included cryotherapy, curettage, and electrodessication. Liquid nitrogen cryotherapy historically was the most common treatment option but had an increased risk of hypopigmentation and hyperpigmentation, especially in patients with skin of color. A recent ex-vivo study performed by Friedman et al. comparing the toxicologic impact of Eskata versus cryosurgery on Fitzpatrick V reconstituted human epidermal equivalents revealed that Eskata promotes greater melanocyte preservation than does cryosurgery.⁴ The current available data illustrates how Eskata provides the safest and most efficacious treatment for asymptomatic raised SKs. Its success in clinical practice will be highlighted in the following case studies.

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Clinical Experience With 40% Hydrogen Peroxide Topical Solution for the Treatment of Seborrheic Keratosis

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ABSTRACT

Despite reassurances about the benign nature of seborrheic keratoses (SKs), patients often request treatment due to cosmetic concerns or for symptomatic relief when SKs become irritated or pruritic. Treatment options include cryotherapy, surgical techniques, and topical therapies. In this study, we present two patients with SKs located on their face and neck who received in-office treatment with 40% Hydrogen Peroxide Topical Solution (Eskata™, HP40), a new FDA-approved topical therapy that has demonstrated efficacy in phase 3 trials. Compared to non-topical, more invasive techniques, HP40 may lead to less pigmentary changes, and may be more efficacious for SKs on the face and neck. Both patients received two treatment courses of HP40, which resulted in positive therapeutic outcomes, including the absence of scarring and pigmentary changes. In addition to the case presentations, we will discuss considerations for appropriate administration of HP40 to maximize clinical outcomes.

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INTRODUCTION

As one of the most common benign lesions, over 83 million Americans are estimated to be affected by seborrheic keratoses (SKs).^{1,2} The prevalence of SKs increases with age – nearly 100% of patients over 50 years old have SKs, with the average number per patient ranging from 9 to 23.^{3,4} Excluding the palms, soles, and mucous membranes, SKs can occur anywhere on the body.⁵ These benign epithelial tumors present as round to oval, sharply demarcated papules or plaques that appear “stuck on.”⁶

Despite being prevalent, the pathogenesis of SKs is not fully elucidated. Investigation of the molecular mechanisms identified at least two mutations, in fibroblast growth factor receptor 3⁷ and the oncogenic phosphoinositide 3-kinase pathway,⁸ that may influence the development of SKs. Additionally, increased cyclin-dependent kinase inhibitor p16 and anti-apoptotic bcl-2 may mediate inhibition of apoptosis in seborrheic keratinocytes.^{9,10} The human papillomavirus (HPV) has also been proposed to influence the formation of SKs given one study found HPV DNA in 76% of non-genital SKs, but the authors were skeptical about HPV being a true causative factor given multiple HPV types were found in one specimen.¹¹ Further, HPV can be found in normal skin.¹⁰ Similar to the pathogenesis, the etiologic risk factors for SKs are not completely understood. Increasing age is a known risk factor as demonstrated by numerous prevalence studies.^{3,4} Ultraviolet light exposure may also increase the risk of SKs, but the evidence is conflicting with two studies showing that SKs are associated with sun exposure,^{3,4} but another study finding that they are not.¹² Finally,

friction may contribute to the development of SKs as they often occur in intertriginous areas.⁵

Patients often desire treatment for SKs out of concern that the skin finding is something serious, for cosmetic reasons, or for symptomatic relief as they can become irritated, painful, or pruritic.^{5,13} SKs are typically diagnosed clinically, but histologic confirmation is recommended for atypical, inflamed, or changing lesions.⁶ In these cases, a shave excision should be done to preserve tissue for diagnosis.⁵ Table 1 presents the current treatment options for SKs, including cryotherapy, surgical techniques, and topical therapies. Cryotherapy is the most common treatment,⁵ however, this therapy and the surgical techniques presented in Table 1 can lead to pigmentary changes, especially in patients with Fitzpatrick Skin Type IV-VI.⁵ Cryotherapy and surgical techniques can also cause bleeding, pruritus, or scarring.^{5,14-21} To avoid these adverse effects, various topical therapies have been utilized to treat SKs (Table 1). The efficacies of keratolytics including ammonium lactate, imiquimod, and tazarotene have been examined but overall, these therapies had limited success in small clinical trials.^{2,22,23} Topical vitamin D analogs have also been used, but similarly, these had limited efficacy for treating SKs.^{2,24} Given the inadequacy of existing topical therapies, safe and effective non-invasive therapies are still needed. One novel therapy is BL-5010, a combination of trichloroacetic acid and formic acid. In a phase I/II open-label trial, a single treatment with BL-5010 resulted in a complete response in 90% of patients and partial response in 7% of patients six months after application (n=60).²⁵ The medication was well-tol-

TABLE 1.

Surgical Therapies		
Type	Description and Outcomes	Side Effects
Liquid nitrogen cryotherapy	<ul style="list-style-type: none"> Destroys SKs by forming ice crystals that damage cells and via an inflammatory mechanism that is not fully elucidated.^{28,32} Useful for thin, small SKs in non-cosmetically sensitive areas; can be combined with other therapies for thicker SKs.⁵ Success depends on SK thickness, freezing time, and number of freeze/thaw cycles;^{2,14,15} >1 treatment may be needed for clearance.⁵ Clinical and histologic clearance was seen in 15/15 patients in one trial.² In another trial, residual disease was more common with cryotherapy than curettage, but patients preferred cryotherapy given less wound care was required.¹⁶ 	Pain, burning, bleeding, blistering, scarring, or pigmentary changes, including post-inflammatory hyperpigmentation and permanent depigmentation from melanocyte destruction. ^{5,17}
Electrocautery	<ul style="list-style-type: none"> Destroys SKs via electrodesiccation (electrode applied to skin) or electrofulguration (electrode held near skin).⁵ Useful for small lesions in patients with dark skin (may have a lower risk of pigmentary changes than cryotherapy).⁵ 	Pain, pigmentary changes, or scarring. ¹⁸
Curettage	<ul style="list-style-type: none"> Useful alone for small, thin lesions or in combination with electrocautery or cryotherapy for thicker lesions. Requires post-procedure wound care.¹⁶ 	Pain (less than with cryotherapy); scarring or hypopigmentation (higher risk than cryotherapy). ¹⁶
Shave excision	<ul style="list-style-type: none"> Allows for rapid removal of a single SK and preserves tissue for diagnosis.⁵ Requires local anesthesia and wound care after the procedure, but has acceptable cosmetic outcomes with proper post-procedure care.⁵ 	Pain, pruritus, bleeding, infection, or scarring. ¹⁹
Laser therapy	<ul style="list-style-type: none"> Ablative and non-ablative lasers have been used to destroy SKs.¹⁴ Useful for large surface areas or multiple SKs.^{14,15} 755-nm alexandrite laser was used to treat hundreds of SKs in one patient with a good cosmetic outcome¹⁵ and in a small study (n=13) where it resulted in complete resolution of SKs.²⁰ 532-nm diode laser cleared 96% of SKs in one study (n=326).²¹ 	Pain, scarring, or pigmentary changes (lower risk with non-ablative lasers than ablative lasers). ^{14,15,20,21}
Topical Therapies		
Type	Description and Outcomes	Side Effects
40% H2O2	<ul style="list-style-type: none"> Mechanism likely involves the oxidizing effects of H2O2.²⁶ FDA-approved to treat raised SKs, but not covered by insurance.²⁶ Less cytotoxic to melanocytes than cryotherapy in an ex vivo model,³¹ so it may be useful to treat SKs in cosmetically-sensitive areas. >1 treatment may be needed for clearance.²⁶ 	Burning, scaling/crusting, erythema, pruritus, erosions, pigmentary changes, or scarring. ²⁶
BL-5010	<ul style="list-style-type: none"> Combination of trichloroacetic acid and formic acid.²⁵ Proposed mechanism: in situ cell fixation leads to cell death and detachment of SKs.²⁵ Phase I/II open-label trial: single application (n=60) resulted in SK detachment in 97% of patients 30 days later. Six months later, 90% experienced a complete response and 7% a partial response. Treatment was well-tolerated overall.²⁵ 	Burning, pruritus, bleeding, scaling/crusting, erythema, or edema. ²⁵
Vitamin D analogs	<ul style="list-style-type: none"> Affects differentiation and apoptosis of keratinocytes.^{2,33} Various ointments were applied 1-2 times/day for 3-12 months (n=116); only 30.2% of patients experienced 80-100% decrease in volume.²⁴ In another trial (n=15), 0.005% calcipotriene ointment did not produce any clinical improvement.² 	Erythema, burning, or irritation have been reported, but no side effects occurred in the trials. ^{2,24}
0.1% Tazarotene cream	<ul style="list-style-type: none"> Binds retinoic acid receptors in keratinocytes leading to anti-proliferative effects.² Twice daily use resulted in clinical and histologic clearance in 7/15 patients (compared to 15/15 with cryotherapy).² 	Burning, pruritus, or erythema (but tolerance to side effects develops with continued use). ²
Imiquimod 5% cream	<ul style="list-style-type: none"> Immune response modulator that is effective for other skin neoplasms.^{2,6} Did not result in clinical improvement in one trial (n=15),² but was successful for one patient with SKs positive for multiple HPV types.²² Therefore, it may only be effective for SKs with HPV DNA.⁶ 	Erythema, burning, or ulceration (can persist for >1 month). ²
12% Ammonium lactate	<ul style="list-style-type: none"> Keratolytic that decreased SK height compared to vehicle but did not affect SK length, surface characteristics, and color; only cleared two SKs after 16 weeks of twice daily use (n=58).²³ 	Burning or erythema. ³⁴

erated but the authors did not discuss the risks of pigmentary changes or scarring. Larger studies are needed to further examine BL-5010's safety and efficacy. Another new therapy is a stabilized, high concentration hydrogen peroxide (40% H₂O₂) solution (Eskata™, HP40), which is the first FDA-approved topical therapy for raised SKs.²⁶

HP40 is applied topically with a single-use, disposable applicator pen that can be used to treat multiple SKs in one setting (up to 10 if the SKs are small based on the author's experience). Per the manufacturer's protocol, the H₂O₂ solution is rubbed onto each SK in a circular motion to uniformly coat the surface. This process is repeated three additional times for each SK, separating each application by approximately one minute. After three weeks, another treatment may be needed if the SKs do not completely disappear. The efficacy of HP40 for the treatment of four SKs per patient was examined in two Phase 3 trials (n=937). Compared to vehicle, 1-2 applications of HP40 resulted in a higher mean per-patient percentage of clear/nearly clear SKs (51% for HP40 versus 7% for vehicle).²⁶ A further sub-analysis showed that the percentage of clear/nearly clear SKs was higher for the face (65%) than for other locations (46% for trunk, 38% for extremities).²⁷

In this case series, we present two patients who received in-office treatment with HP40 for SKs located on their face and neck. This novel topical therapy resulted in positive therapeutic outcomes for both patients presented. Further, we will discuss practical considerations for using HP40 based on the author's experience with this product.

CASE 1

A 52-year-old Caucasian female with Fitzpatrick SkinType II presented for treatment of numerous SKs on her face and neck. A few years ago, she received treatment for SKs located on her neck with cryotherapy, but she was disappointed with the hypopigmented scars left behind. The patient was deemed to be a good candidate for HP40 treatment given she had a previous negative experience with cryotherapy and had multiple lesions in cosmetically-sensitive areas. A total of 9 SKs on her face, hairline, and neck measuring from 5 mm to 1.2 cm (Figure 1A) were treated with one HP40 pen according to the product's protocol (Figure 1B). The patient was evaluated 20 days later and given the presence of residual disease (Figure 1C), all 9 SKs were re-treated following the same procedure. The patient was seen again 106 days after the initial treatment; complete resolution of all the SKs was appreciated on exam (Figure 1D) and the patient was happy with the outcome.

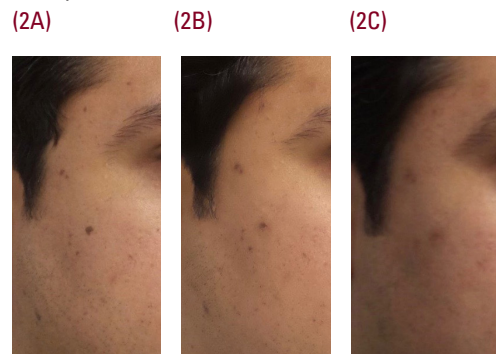
CASE 2

A 37-year-old Hispanic male (Fitzpatrick SkinType IV) presented for treatment of several dark, painless lesions on his face that

FIGURE 1. SKs on the face and neck, Case 1. (1A) Before first HP40 treatment. (1B) Immediately after first HP40 treatment. (1C) 20 days after first HP40 treatment. (1D) Final result, 106 days after first HP40 treatment/86 days after second HP40 treatment.



FIGURE 2. SKs on the face, Case 2. (2A) Before first HP40 treatment. (2B) 42 days after first HP40 treatment. (2C) Final result, 70 days after first HP40 treatment/28 days after second HP40 treatment.



were bothersome in appearance and grew slowly over the past several years. On exam, the patient had multiple well-defined, brown, raised papules measuring 4 mm to 8 mm on the right side of his face, consistent with SKs (Figure 2A). Considering the location of the SKs and the patient's skin type and age, topical treatment with HP40 was recommended. The SKs were

treated with one HP40 pen according to the manufacturer's protocol. At a follow-up visit six weeks later (Figure 2B), residual disease was present, so all the SKs were retreated with HP40. Four weeks later (70 days after the first treatment), the SKs were nearly clear without scarring, an outcome that pleased the patient (Figure 2C).

DISCUSSION

HP40 was recently FDA-approved to treat raised SKs and as demonstrated by the two cases presented here, this in-office treatment can lead to positive therapeutic outcomes for SKs located in cosmetically-sensitive areas. The mechanism by which HP40 destroys SKs is not fully understood, but it likely utilizes the oxidizing potential of H₂O₂.²⁸ H₂O₂ can directly damage cell components as a reactive oxygen species and form hydroxyl free radicals to exert further oxidative damage.²⁹ Applied at supraphysiologic doses, HP40 delivers a fraction of the dose through the stratum corneum (SC) to the epidermis, where it can generate free radicals by overcoming the skin's antioxidant capabilities and initiate cellular apoptosis and necrosis. Because of this mechanism, HP40 should not be applied to open or infected SKs where the SC is compromised. The SC protects deep tissue from high concentration H₂O₂ so without this barrier, H₂O₂ can cause rapid death of nearby cells.³⁰ However, when used properly in phase 3 trials, side effects of HP40 were limited to local skin reactions, the majority being mild to moderate.²⁶ Scarring, hypopigmentation, and hyperpigmentation occurred in less than 1%, 3.0%, and 7.8% of sites treated with HP40, respectively.²⁶ Although, nearly all of the participants were Fitzpatrick Skin Types I to IV, so the effect of HP40 on darker skin is less clear.²⁶ In an ex vivo model of human Fitzpatrick Skin Type V, HP40 was less toxic to melanocytes compared to cryotherapy.³¹ Therefore, HP40 may be superior to cryotherapy for skin of color, but large, controlled studies including multiple skin types are needed to compare these therapies.

In support of HP40's potential to minimize the risk of scarring and pigmentary changes, the patient in Case 1 was previously treated with cryotherapy, which led to hypopigmented scarring. However, as seen in Figure 1D, there was no evidence of scarring or hypopigmentation from HP40 after over three months. The patient in Case 2 with Fitzpatrick Skin Type IV was similarly spared of these adverse effects. While HP40 still has a small risk of scarring and pigmentary changes, this is a good option to discuss with patients who want to minimize the side effects from treating SKs in visible skin areas.

Selecting a therapeutic strategy for SK removal requires consideration of the location of SKs as well as the patient's skin type and expectations of what will be left behind after removal. Given HP40 is not covered by insurance and multiple treatments may be needed, patients with SKs in non-cosmetically sensitive areas may prefer treatment with cryotherapy, curettage, or

electrodessication. However, patients with SKs in cosmetically-sensitive areas like the face and neck, particularly those with dark skin types, may benefit from a topical therapy like HP40 that is less cytotoxic to melanocytes and the neighboring epidermis.³¹ This is especially true if patients are dissatisfied with previous treatments. Further, as demonstrated by phase 3 trials²⁶ and based on the author's experience, raised SKs on the face and neck respond especially well to treatment with HP40.

In addition to instructions provided by the manufacturer, the following practical considerations based on the author's experience may be helpful when using HP40. It is important to apply firm pressure and cover the entire lesion, while staying within a 2 to 3 millimeter margin of the SK to avoid contact with normal skin. Four treatment cycles are recommended for each SK, but if the patient experiences 6 to 7 or more pain on a scale of 0 to 10, the treatment should be terminated. Additionally, when treating SKs near the orbital rim, some eyelid swelling is expected; reassure the patient that this usually resolves in a few hours.

Overall, HP40 is a new therapeutic option for SKs that can be discussed with patients. As demonstrated by the cases presented here, HP40 is particularly useful for SKs on the face and neck and may avoid the scarring and hypopigmentation that can occur with cryotherapy. Future examination of HP40 in patients with dark skin types is needed to confirm our suspicion that HP40 may lead to less pigmentary changes than non-topical, invasive therapies.

DISCLOSURE

The authors have no conflicts of interest.

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Enhancing Outcomes in Seborrheic Keratosis: Using a Novel Treatment Solution

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ABSTRACT

Seborrheic keratosis (SK) is an extremely common benign cutaneous lesion that often appears on individuals older than the age of 50. SK lesions can appear in numerous clinical variations, but typically, SKs present with a well-demarcated, “stuck-on” appearance having a waxy or keratotic surface. Even though SK lesions are usually benign, many individuals elect for SK treatment or removal due to cosmetic concerns. One study regarding SK appearance reported that 61% of women tried to conceal the appearance of the SKs by using certain hairstyles, make-up, and clothes. Conventional treatment for SK lesions ranges from cryosurgery to curettage. Although these removal methods are effective for SK treatment, each method contains a potential for side effects such as pigmentation changes, scarring, and discomfort before and after the procedure. Due to many of these concerns, patients prefer topical treatments for SKs, which has led to a new emerging topical containing hydrogen peroxide topical solution 40% (HP40; Eskata™). Here, we report the methods and results from an HP40 treatment for two individuals, each over 70 years old. Application of the topical solution was performed on each target SK, up to four times, with a 20-second application and 1 minute between applications. The two participants reported moderate success of HP40 in the removal of their SKs with minimal adverse effects.

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INTRODUCTION

Seborrheic keratosis (SK) is one of the most common cutaneous lesions that a dermatologist will encounter daily.¹ SKs can develop anywhere on the body excluding the soles, palms, and mucous membranes.¹ SKs are benign epithelial tumors that present as “stuck-on,” well-demarcated, waxy, or verrucous papules or plaques that consist of varying coloration from flesh-colored to heavily pigmented (brown, yellow, grey, or black).² SKs appear most commonly in middle-aged individuals, 31-50 years (42%), and the number and size of SKs increases with age.³ One study conducted in Australia reported that the prevalence of SKs increased from 12% of individuals between 15-25 years old to 100% in individuals over the age of 50.⁴ Within the same study, the average number of lesions increased from 6 lesions per individual in the age group of 15-25 years old to 69 lesions per individual in the group that was 75 years or older.⁴ Even though studies indicate that the incidence of SKs increases with age, the etiopathology is still misunderstood.⁵ Age, chronic ultra-violet (UV) exposure, and genetic inheritance are commonly proposed hypotheses that are associated with the occurrence of SKs. SKs can appear anywhere on the body, but one study of 406 total patients found the majority of SKs were found on the truncal region (chest, back, shoulders, abdomen) in approximately 85% of patients, and the face in approximately 68% of the patients.⁶

Typically, SKs present with dermoscopic findings such as fissures and ridges, hairpin vessels with white halo, comedo-like

openings, and milia-like cysts.⁷ Fissures and ridges are terms used to describe the linear grooves produced in the epidermis that present as thick, curved lines giving the lesion a “brain-like” appearance.⁸ Hairpin vessels are characterized by linear vessels that form a U-shape with a bend at one end resembling a hairpin with a whitish halo surrounding the vessels.^{7,8} Comedo-like openings are keratin-filled invaginations of the epidermis and appear as black or brown, roundish structures.^{7,8} Finally, milia-like cysts are characterized by round white to yellowish globules.^{7,8}

The presence of these dermoscopic findings correspond with the histopathologic changes within the epidermis and dermis. The thickened, papillomatous surface of the epidermis forms grooves and clefts that can be filled with keratin. The intralesional cysts of loose filled keratin cleft are called pseudohorn cysts and correlate to the appearance comedo-like openings of the SK.^{7,9,10} The presence of intraepidermal cysts signify milia-like cysts, while the appearance of hairpin vessels are caused by enlarged capillaries within the dermis.^{7,9,10}

The majority of SKs are typically asymptomatic and benign, therefore, do not require removal, but patients will often choose to have these lesions removed. The truncal regions are subject to frequent contact by clothing fabric, which may cause SKs to become symptomatic resulting in irritation, pain, bleeding, or itching.¹¹ Patients also elect for removal of SKs for cosmetic reasons, often stating a desire to improve their quality of life

and maintain a more youthful appearance since SKs are often termed “age-spots.”¹¹ One study specifically reported that 61% of the female patients attempted to conceal or disguise the appearance of SKs by using specific clothing, hairstyles, and even make-up.⁶ The majority of SKs are removed or treated for cosmetic purposes. Treatment methods include cryosurgery, electrodesiccation, shave excision, curettage, and emerging topical treatment, such as hydrogen peroxide topical solution (HP40) (Eskata™, Aclaris Therapeutics, Wayne, PA).

The most common traditional technique for SK removal is with the use of cryosurgery.¹² Although the specific mechanism of cryosurgery is not fully understood, cryosurgery destroys the SK lesion by inducing intracellular ice crystal formation within the benign tissue, which leads to various inflammatory responses.¹³⁻¹⁵ Cryosurgery can be effective for SK removal depending on characteristics of the lesions and patient, freezing technique, freezing time, and the number of freeze/thaw cycles.^{11,12} Larger and thicker lesions will often require extended freezing durations or more treatment sessions compared to small flat SKs.¹¹ Another commonly employed technique used by dermatologists is electrosurgery, which uses an electrode held at a certain distance away from the skin that creates a local energy delivery specifically destroying the epidermal tissue.¹¹ Curettage is another technique that can be used in combination with both electrosurgery or cryosurgery to remove any remaining SK lesions.¹¹ A study done by Wood et al. reported that 64% of the patients who had their SK lesions treated by cryosurgery or curettage, preferred cryosurgery due to a decreased amount of postoperative wound care after cryosurgery.¹⁶ Adverse effects such as erythema, slight bleeding, blister formation, and pain are typically found at the treatment site after both treatments. However, both treatments can cause potential long-term complications such as scarring, permanent pigmentation changes (hyper or hypopigmentation), infection, and lesion recurrence.¹⁷ Patients with darker skin types have an increased likelihood of pigmentary changes, recurrence, and scarring compared to individuals with a lighter skin type.^{11,15}

Due to many of these concerns of adverse effects and postoperative care, patients have expressed interest in a noninvasive, safe, cosmetically acceptable treatment for SK removal.¹⁸ Patients indicated that they avoided the removal of SKs due to potential long-term side effects such as scarring, discomfort, pain, and post-treatment hypo or hyperpigmentation.⁶ Recently, the US Food and Drug Administration approved a hydrogen peroxide topical solution 40% (HP40; Eskata) as the first and only topical treatment for raised SKs. The high concentration of hydrogen peroxide within the topical solution can produce reactive hydroxyl radicals and other oxygen species that cause oxidative damage to the SKs.¹⁷⁻²⁰ However, the exact mechanism of action for HP40 is unknown. Although a similar adverse effect profile as traditional therapies may be seen using HP40, a

recent ex vivo study compared cryosurgery and HP40, concluding that HP40 caused less cytotoxicity and reduced melanocyte damage than cryosurgery.²¹ The authors suggested that HP40 is a safer option for SK removal that features a decrease in posttreatment pigmentary alteration.^{19,21} Two randomized, double-blind, placebo-controlled studies evaluated the safety and efficacy of hydrogen peroxide topical solution on patients with seborrheic keratosis. After day 106, lesions undergoing two treatments with hydrogen peroxide resulted in scarring, hypopigmentation, and hyperpigmentation in <1%, 3.0%, and 7.8% of lesions, respectively.²² The authors also found that the percentage of subjects achieving clearance of all four target lesions at day 106 were 4% and 8% while the percentage of subjects in which 3 of 4 target lesions were “clear” was 13% and 23%.²² Here, we report the methods and results from an HP40 treatment for two individuals.

CASE REVIEWS

Patient one, a 73-year-old female with Fitzpatrick skin type III, stated that she has an extensive history of sun exposure throughout her youth and adulthood. The individual reported that she began to notice the appearance of her SKs approximately 30 years ago on her chest and back region, and she had seen that the number and size of the SKs slowly began to increase over the years. Patient one stated that she has been continuously bothered by the appearance of the SKs indicating that they appear “ugly and unappealing,” and made her skin seem “aged,” which affected how she perceived her image. She expressed dislike in the color and texture of the SKs, and due to the appearance, she believes that when people saw her, they thought she was older than her actual age. She also noted that the SKs are sometimes irritating, producing discomfort. Patient one explained that she previously had traditional treatments, including cryosurgery, and excision, for the cosmetic removal of her SKs, after which she experienced moderate to severe adverse effects. Adverse effects included erythema, blistering, tenderness, and hypopigmentation that mostly resolved after 1 week to 2 months. She indicated that she had noticed some residual post-treatment hypopigmentation in the areas treated with traditional therapies. The patient explained that she scheduled an appointment to talk about the removal of her SKs, and during the appointment, she was introduced to the hydrogen peroxide topical solution called Eskata. The patient stated that she became very interested in Eskata due to it being an alternative, non-invasive treatment compared to the traditional treatment. The patient revealed that she tolerated the initial treatment well with a slight amount of irritation. The patient expressed after the treatment there were very mild adverse effects such as, blistering, redness, and tenderness, for approximately 1 week with no evidence of post-treatment hypopigmentation. In comparing HP40 with her previous treatments, the patient stated the side effects with the HP40 were less overall, but she noted the areas targeted were smaller compared to her other

treatments. The patient indicated that she had no trouble caring for the areas treated and that she believes that the HP40 was effective in the removal of her SKs. She observed that a majority of the treated SKs completely disappeared, and the ones that did remain after treatment had a reduction in size. The patient expressed that she was delighted with the outcome and that the treatment has improved her lifestyle. The patient proclaimed that she expresses more confidence and rejuvenation as her skin appears “more youthful and feels younger” since the treatment.

Patient two, a 75-year-old male with Fitzpatrick skin type III, expressed that he had an extensive history of sun exposure throughout his youth and adulthood. Patient two reported that he first noticed his SKs approximately 7 to 10 years previously on his back and chest region. The patient stated that he had never been embarrassed by the appearance of SKs; however, he did express that they were “aesthetically, very unpleasant” and made him feel much “older.” The patient stated that he had never previously tried any treatments for the cosmetic removal of his SKs but became very interested in the treatment of HP40 after hearing about the potential of this non-invasive treatment. Specifically, the patient expressed that the reduction of potential adverse effects of HP40 compared to other traditional therapies was appealing. He stated that he never tried any conventional treatment due to his concerns with potential scarring and post-treatment pigmentation changes. The patient stated that he tolerated the initial treatment of HP40 well with no sign of discomfort or irritation, and that he does not recall any pain or adverse side effects after the procedure. The patient stated that within approximately 3 days, two of the treated lesions were completely gone. Altogether, the patient indicated that two of the target lesions were clear, two were partially destroyed, and two were left unaffected. Even with this result, the patient stated that he was thrilled with the outcome, and that the targeted treatment sites appear more youthful and appealing to the eye.

The two patients, both adults over the age of 60, presented with multiple (ranging from 5-6) benign, clinically typical SKs on the neck and chest region as seen in Figure 1.

Lesions ranged from 1 to 1.5 mm in thickness and 5-15 mm in length and width. The SKs were free from any hair that could interfere with the application and diminish the effect of the topical solution. Prior to the application of the topical solution, each targeted SK was disinfected and degreased with alcohol. The treatment was applied by a physician using the single-use, disposable applicator provided with Eskata. Topical solution was applied onto the targeted SKs, and each SK was rubbed, using the angled soft tip of the disposable applicator, with moderate pressure in a circular motion for approximately 20 seconds. The application process was designed to saturate the lesion with

FIGURE 1. Clinically typical SK on the neck and chest.



the HP40 solution including under any lesion edges using the tapered applicator tip. Treatment cycles were repeated up to 4 times per targeted SK and, according to the instructions for use for Eskata, each targeted lesion requires 60 seconds between each application. Only one treatment session was given for each patient. In some cases, two or more may be required for best results.

DISCUSSION

Seborrheic keratosis can impose a substantial burden on individuals due to their unappealing appearance, potentially accompanied by medical or cosmetic concerns as well. Many individuals express dissatisfaction with the presence of SKs and seek removal of these benign lesions. From a survey of 406 patients who sought treatment for their SKs, 53% stated they did not like how SKs looked, 33% reported that they were embarrassed by the appearance of SKs, and 31% indicated they believed the presence of SKs resulted in an older appearance.⁶ Furthermore, 61% of surveyed female patients stated they have actively tried to disguise the presence of SKs with clothing, make-up, and jewelry.⁶

Similarly, both participants described here indicated they were bothered with the appearance of their skin and uncomfortable with how people perceived them. The patients stated that the presence of SKs hindered their confidence and negatively affected the quality of their life. The individuals became interested in HP40 treatment after learning about the potential benefits and reduced risks compared to traditional therapies for SKs including pigmentary changes, erythema, edema, crusting, and blister formation.^{19,21,22} While one individual stated that he had no side effects during and after treatment, the other said that she felt no pain during the initial treatment and after, only mild erythema, tenderness, and minor pain that lasted approximately 1 week. Each expressed no evidence of post-treatment permanent pigment alterations, and many of the targeted lesions were clear or partially clear within 1 to 2 weeks after treatment (Figure 2). Ultimately, both individuals expressed satisfaction with the pro-

FIGURE 2. Partially clear within 1 to 2 weeks after one treatment session with HP40.



cedure. It is important to note that in this application process, only one treatment session was administered per patient. The package insert for Eskata suggests that another treatment may be administered after approximately 3 weeks, if the first treatment did not completely clear the lesions.

In these cases, HP40 produced sufficient and satisfactory results for destruction of SKs while yielding minimal adverse effects. However, HP40 contains a high concentration of hydrogen peroxide, potentially leading to oxidative damage to areas of the skin with increased irritation, pain, and erythema, if treated improperly. To maximize successful clearance of SK and minimize adverse effects, physicians and other practitioners can consider the following techniques.

The first key to treatment success comes with thorough saturation of the lesion during each application. The provider applying the topical solution must treat the lesion with the recommended number application (four) sessions to achieve the optimal clinical endpoint, which is a thorough whitening of the lesion and surrounding skin (approximately 1 millimeter). The affected area should display no evidence of bleeding, erosion, or blister formation. If one of these adverse effects occurs, the lesion has been saturated with too much topical solution, and the provider should move on to a different lesion. The lesion surface should be uniformly wet without any excessive running or dripping onto the surrounding area of the skin. If any residual solution drips onto the surrounding unaffected skin, the provider should remove the excess solution with a clean absorptive wipe. It is important to use a paper towel or tissue because residual solution may still reside on the unaffected skin, which may increase the risk of adverse effects. For best results, allow the lesion to completely dry before another application. The provider should

wait the recommended 1 minute between applications and ensure that the topical solution is applied only to targeted lesions.

After treatment with HP40, it is important to leave each lesion dry without applying a dressing or ointment for 4 hours so the hydrogen peroxide solution will have maximum effect. After 4 hours, the patient should apply an occlusive dressing to the treated areas. The targeted areas should remain covered with a bandage and lubricated as needed until the SKs slough off naturally. HP40 is a novel FDA approved treatment for seborrheic keratosis. With careful patient selection and attention to best-practice treatment technique, patients can benefit from removal of unsightly lesions with minimized adverse effects.

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